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Edwin H. Lennette

PIONEER OF DIAGNOSTIC VIROLOGY WITH THE  
CALIFORNIA DEPARTMENT OF PUBLIC HEALTH

With Introductions by  
Harald N. Johnson, M.D.  
and  
David A. Lennette, Ph.D.

An Interview Conducted by  
Sally Smith Hughes  
in 1982, 1983, 1986

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EDWIN H. LENNETTE, M.D., Ph.D.

*Portrait by Paul Bishop*



Edwin H. Lennette, M.D., Ph.D. Died October 1, 2000

San Francisco Chronicle October 28, 2000

**LENNETTE, Edwin H., M.D., Ph.D.** — October 1, 2000, in Walnut Creek. (age 92). Dr. Lennette's wife of 50 years, Elizabeth H. Lennette, died in 1991. He is survived by his children, Edwin Paul Lennette, Ph.D., of Thousand Oaks, and David A. Lennette, Ph.D., of Alameda, and by his three grand-children, Michael, Andrew and Marie Lennette. His sister, Henrietta J. Ede of Pitts- burgh, PA died in 1979.

Dr. Lennette was a member of the Univer- sity of Chicago Class of 1931. He received a Ph.D. from the University of Chicago in 1935 and his medical degree from Rush Medical College in 1938. Dr. Lennette joined the International Health Division of the Rockefeller Foundation in New York City and was assigned to Brazil in 1941 to work on yellow fever and encephalitis. He was reassigned to their laboratory in Berkeley, CA to work on hepatitis and encephalitis in 1944. In 1947 he accepted appointment as Director of the Viral and Rickettsial Disease Laboratory of the California Department of Health Services in Berkeley, in which capacity he served until his retirement in 1978. This laboratory, which he was instru- mental in developing, was the first clinical virology laboratory of its kind in the United States, dedicated to serving the needs of the medical and public health communities. Following retirement, Dr. Lennette re- mained active as a consultant and, until 1998, as the President of the Public Health Institute in Berkeley, of which he was a founding member. Dr. Lennette was an internationally recognized expert in clinical virology, and belonged to many scientific and professional associations, serving as national president of three of them.

Memorial services are pending. Family requests contributions to the Macular Dis- ease Center, Development Office, Jules Stein Eye Institute, 100 Stein Plaza, UCLA, Los Angeles, CA 90095-7000.

Colonial Chapel  
2624 High Street  
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TABLE OF CONTENTS -- Edwin H. Lennette, M.D., Ph.D.

INTRODUCTION by Harald N. Johnson, M.D.	i
INTRODUCTION by David A. Lennette, Ph.D.	iv
INTERVIEW HISTORY	vi
BRIEF BIOGRAPHY	x
I FAMILY BACKGROUND AND EDUCATION	1
Grandparents and Parents	1
Grammar School and High School	3
The University of Chicago, 1927-1936	7
Virology Instruction in the Thirties	13
Paul Hudson's Yellow Fever Research	15
Virology Instruction in the Thirties (continued)	17
Polio Research	20
II EARLY CAREER	33
Washington University, School of Medicine, St. Louis, 1938-1939	33
Margaret Smith and Cytomegalovirus	35
Encephalitis Research	36
The International Health Division of the Rockefeller Foundation, 1939-1946	37
Rockefeller Personalities and Research	40
Influenza Studies	41
Early Virological Tests	42
Debate Over the Nature of the Virus	51
Encephalitis and Yellow Fever in Brazil, 1941-1945	54
Hilary Koprowski	63
Interferon	65
The Use of Suckling Mice in Viral Assays	66
The Rockefeller Foundation Laboratories at the California State Department of Public Health, 1944-1946	68
Monroe Eaton and the Eaton Agent	68
Encephalitis Studies	71
Camp Detrick, Maryland, 1946-1947	74
III THE VIRAL AND RICKETTSIAL DISEASE LABORATORY, CALIFORNIA DEPARTMENT OF PUBLIC HEALTH	75
The Development of Diagnostic Virology	76
Wendell Stanley's Virus Laboratory at the University of California	80

Location, Construction, and Design of the Health Department Laboratories	82
The Virus Laboratory's Association with other Institutions	88
Karl Meyer	89
Encephalitis Research	91
Training Physicians in Virological Techniques	94
Current Work on Three Books	98
Q Fever	100
Hepatitis Research	110
Training Physicians in Virological Techniques (continued)	110
The Training Program in Diagnostic Virology	113
The Impact of State Funding Cuts	114
Designing the Virus Laboratory	116
Types of Diagnostic Tests	117
Diagnostic Virology Laboratories Elsewhere	119
The Early Years of Diagnostic Virology	125
New Directions in Public Health	128
Research on Nonpolio Enteroviruses	130
The Identification of New Viruses	133
Reoviruses and Rex Spindlove	137
Respiratory Viruses	141
The Armed Forces Epidemiological Board	141
Tommy Francis' Role in Influenza Research	144
Fort Ord Research	145
Adenovirus Vaccines	147
Poliomyelitis	149
Early Polio Vaccines	150
Tissue Culture	151
Polio Research at the Virus Laboratory	153
The Salk Vaccine Field Trials	155
The Sabin Vaccine	168
Nathalie Schmidt's Polio Research	172
Cancer Research	175
The New Laboratory Building and Staff Recruitment	176
Robert Huebner, the National Cancer Institute, and the Viral Cause of Cancer	179
Fads and Fancies in Cancer Research	182
Evolution of the National Institutes of Health	184
Rubella Research	186
The Premarital Test for Rubella	187
Diagnostic Kits	188
The Premarital Test for Rubella (continued)	189
New Techniques and Rapid Diagnosis	190
Hepatitis Research (continued)	192
Laboratory Personnel and Miscellaneous Research	193
Robert Magoffin and Laboratory Administration	194
More on Rex Spindlove and the Reoviruses	195
Lyndon Oshiro and Electron Microscopy	196

Jack Schieble, James Chin, and the Fort Ord Studies (continued)	197
Harald Johnson	200
Hilary Koprowski and Subacute Sclerosing Panencephalitis	202
More on Cancer Research	204
Water Virology	205
Cytomegalovirus (continued)	207
Varicella	209
Editorial Efforts	209
More on Viral Diagnosis	215
Laboratory Funding	218
The Rockefeller Foundation	218
The State of California	219
The National Institutes of Health	223
The California Public Health Foundation	228
The Training Program in Diagnostic Virology (continued)	232
Changing Emphasis in Microbiological Education	237
Relations with the University of California, Berkeley	239
The Reputation and Accomplishments of the Virus Laboratory	240
More on Wendell Stanley	243
Concepts of the Virus	244
Recombinant DNA	249
Administrative Duties	254
Professional Associations	256
The Tissue Culture Association	256
The W. Alton Jones Cell Science Center	259
The American Society for Microbiology	261
The Federation of American Societies for Experimental Biology	268
The Armed Forces Epidemiological Board	269
The Wooldridge Committee	271
The U.S.-Japan Cooperative Medical Science Program	271
Consultant to the Communicable Disease Center, Center for Disease Control	273
The World Health Organization	274
The National Cancer Institute	277
Maurice Hilleman	279
Edward C. Pickels	281
Frank L. Horsfall	283
Jonas Salk and Albert Sabin	284
Dr. Lennette's Scientific Contribution	287
IV ADDENDUM I: NOVEMBER 13, 1986	288
Q Fever	288
Cancer Research	293
Nathalie Schmidt	294
Administration of the Virus Laboratory	297
Nathalie Schmidt (continued)	300

Virion, Inc.	301
Satisfactions and Contributions	310
V ADDENDUM II: JULY 21, 1987	313
Family Background and Education	313
Paul and David Lennette	315
More on the Virus Laboratory	316
TAPE GUIDE	319a
APPENDIX A--Curriculum Vitae, Edwin H. Lennette	320
APPENDIX B--Bibliography, Edwin H. Lennette	338
APPENDIX C--Citation for the Bronfman Award for Achievement in Public Health	403
APPENDIX D--Presentation of the Wellcome Award	404
APPENDIX E--"Distinguished Alumnus: Edwin H. Lennette, M.D., Ph.D."	406
APPENDIX F--Organization Charts of the California Department of Health Services, 1977 and 1978	407
INDEX	411

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## INTRODUCTION by Harald N. Johnson, M.D.

I first met Dr. Lennette in the 1940s when we were on the staff of the International Health Division (IHD) of the Rockefeller Foundation. After he resigned from the staff in 1946, we met from time to time at scientific meetings. Our close personal and professional association, which continues to the present day, began in the following way.

In 1957 the Rockefeller Foundation began a worldwide project for the study of arthropod-borne viruses. Field laboratories were established in India, South Africa, Trinidad, and Brazil. The Foundation assigned me to India from 1951 to 1954 during the developmental phase of the Virus Research Centre at Poona.

In these years an epidemic of western encephalitis, a disease caused by an arbovirus, occurred in California. Dr. Lennette, who in 1947 had become chief of the Viral and Rickettsial Disease Laboratory of the California Department of Public Health in Berkeley, invited the Rockefeller Foundation to cooperate with the laboratory in a field project on the natural history of the western and St. Louis encephalitis viruses. My tour of duty in India just completed, I was made director in 1954 of the Arthropod-borne Study Project in Berkeley. At the termination of the project in 1972, I became a staff member of the Viral and Rickettsial Disease Laboratory, where I continued my virological research and my association with Dr. Lennette.

In the 1930s, when Dr. Lennette had completed his training in medicine at Chicago, he was appointed to the staff of the IHD. The central laboratory, which was located at the Rockefeller Institute in New York City, was famous for the research studies done there on yellow fever, influenza, and malaria. The main purpose of the IHD was to apply the knowledge obtained from basic science studies at the Rockefeller Institute and elsewhere to the control of specific diseases. The central laboratory pursued studies for improving the methods of diagnosis, treatment, and immunization, and served as a backup laboratory for storage of the infectious agents, preparation of experimental vaccines, and for serological studies to determine their effectiveness.

Dr. Lennette was assigned to the influenza project where he was concerned with the development of the complement fixation test for the detection of antibodies to the virus, methods for the isolation of the virus, and the development of a vaccine for the disease. He was associated with F. L. Horsfall, Jr., E. R. Rickard, Thomas Francis, T. P. Magill, M. D. Eaton, G. K. Hirst, J. P. Fox, and E. G. Pickels, all of whom became well-known scientists.

During the early 1940s Dr. Lennette was posted to the IHD field laboratory in Rio de Janeiro. This laboratory was a cooperative project of the IHD and the Ministry of Public Health of Brazil for the study and

prevention of yellow fever. The field project was to set up a vaccine production unit for the new live virus yellow fever vaccine developed at the New York City laboratory, and to conduct serological studies to determine its effectiveness.

In 1944 Dr. Lennette was posted to the IHD field laboratory at the California Department of Public Health in Berkeley. Dr. W. A. Sawyer, the director of the IHD, had previously been director of the department of laboratories there, where the IHD had established a cooperative field laboratory for the study of influenza viruses and others that might be associated with epidemic respiratory infections. Dr. M. D. Eaton was director of this project.

When Dr. Lennette arrived, there were special studies of influenza A, the newly discovered influenza type B, a chlamydia-type virus called meningopneumonitis virus, and primary atypical pneumonia, a syndrome later found to be caused by a mycoplasma organism. Dr. Lennette subsequently left the IHD to accept an appointment with the army microbiological establishment to direct studies of viruses affecting the armed forces.

Dr. Lennette returned to Berkeley in 1947 to become the director of the Viral and Rickettsial Disease Laboratory. During his long tenure there, he developed a major center for the study of viral, rickettsial, and chlamydial diseases, where virologists from all over the world have been trained and extensive studies completed on the nature of many different infectious agents. It is the quality and accuracy of laboratory diagnosis, methods of isolation of infectious agents, safety procedures, methods of viral preservation and storage, and record keeping that identify a great research institution.

There has been a close association with the School of Public Health of the University of California at Berkeley both in the teaching and research programs. Dr. Lennette has edited many editions of books dealing with viral and rickettsial diseases and virological technique. This in addition to the numerous publications from the laboratory at Berkeley and other laboratories with which he has been associated has made the Viral and Rickettsial Disease Laboratory one of the leading public health laboratories of the world.

Dr. Lennette made my association with the California Department of Health a most pleasant and productive time. Friends for more than forty years, we understand each other and share an abiding interest in training young people for careers in laboratory science. I appreciate the invitations to prepare chapters on methods for several books on virus technology which Dr. Lennette edited. He is an excellent editor and I appreciated his guidance in the preparation of manuscripts. We have shared in the teaching program at the School of Public Health of the University of California at Berkeley. We also share an interest in clinical medicine, and we have been active in the local medical society and in continuing medical education programs.

Our social contacts have been numerous in the course of entertaining local and visiting scientists. My wife, Frances, and I enjoyed the dinners shared when either family entertained visitors at home. Frances remembers her long and pleasant friendship with Elizabeth Lennette who from our arrival in California was most cordial. We miss Elizabeth and mourn her death. Frances and I have enjoyed a long friendship with David and Evelyne Lennette, both distinguished virologists.

Harald N. Johnson, M.D.

November 1987  
Berkeley, California

## INTRODUCTION by David A. Lennette, Ph.D.

I was asked by the Regional Oral History Office to write an introduction for my father's oral history from the perspective of a son who also happens to be a virologist. I admit to having the initial idea for an oral biography of my father, which I hoped would not only document his career in diagnostic virology, but also serve as a diversion after the death of my mother in 1981.

In 1947 my father assumed the direction of the Viral and Rickettsial Diseases Laboratory of the California State Department of Public Health (now the Department of Health Services). I remember the major changes in the activities and the facilities of the laboratory as I was growing up. My impression of the original facility at University Avenue and Acton Street was that it was small and very noninstitutional in atmosphere, almost homelike. Mrs. Alwine van Allen ("Al" to most people), upon whom my father depended for much of the day-to-day supervision of laboratory activities, seemed much more motherly than managerial in her demeanor and expressions. The staff itself was very much like an extended family, with lots of small social occasions. Many functions, such as the annual Christmas parties, were even more memorable because of the effort and co-operation required on everyone's part to produce them.

I remember my father spending many hours poring over the large blueprints of the new facilities under construction on Berkeley Way at Shattuck Avenue. He worked at home seated at a large, but old-fashioned oak desk located in the enclosed sun porch of our home on Bayo Vista Avenue in Oakland. After the move to the new facilities in 1954, the character of the laboratory changed, not dramatically, but rather subtly and over a long period of time. The staff grew larger, and the laboratory sections were spread out over a large area. It was no longer practical to invite the entire staff at one time over to parties at our home, even though it seemed like a very large house to me at the time. The familylike relations among staff did not disappear, but I feel that they gradually became diluted with the growth of the laboratory and the scope of its activities. By today's standards, the staffing has been surprisingly stable. Although many of the original employees have retired in recent years, I still see familiar faces that I grew up among yet at work in the Berkeley laboratory.

I also recall the numerous occasions on which foreign and domestic scientists visited the laboratory, and often our home as well. Some would visit for only a day or two, but many stayed for longer periods, up to several months. I had a chance to meet many of them at our dinner table, as they were routinely invited for dinner, and few declined (my mother had a reputation as an excellent cook). Many of them had interesting stories to tell, but they always seemed to regard my father's laboratory as a place of learning--perhaps not an academic institution, but rather a busy workshop where one could learn and practice the latest tricks of the trade.

I learned to take for granted my father's extensive travels. With the many national and international scientific and advisory committee meetings he attended, it seemed that he was rarely home for as much as a month at a time, except perhaps in the winter. His trips were longer in the earlier years when train travel required more time. With air travel, the shorter transit time was simply replaced with even more frequent trips. Somehow, he did not seem to suffer any ill effects from a travel schedule that would leave most people tired and out-of-sorts. He was always bringing back new ideas and reports on the politics of science at the time.

Together, these experiences convinced me that what took place in the Viral and Rickettsial Disease Laboratory in Berkeley was not routine elsewhere, that it was a unique institution in the development of clinical and public health virology. Under my father's administration, the laboratory led the field of diagnostic virology in its research activities, and trained countless scientists from many nations. My father, with the help of his hand-picked staff, contributed much to its development and its success; I am pleased that I was able to persuade him to tell some of his story herein.

David A. Lennette, Ph.D.  
President, Virolab, Inc.

November 1987  
Berkeley, California

## INTERVIEW HISTORY

Edwin H. Lennette's pioneering contributions in the field of diagnostic virology prompted these interviews conducted by the Regional Oral History Office over a five-year period. Under his tenure (1947-1978) at the Viral and Rickettsial Disease Laboratory of the California Department of Public Health\* in Berkeley, the Virus Lab, as it is familiarly known, became one of the foremost centers of viral diagnosis in the world.

In the interviews Dr. Lennette talks about entering the nascent field of virology in the mid-1930s and associating with many of the early great American virologists, first at the University of Chicago, then at Washington University Medical School in St. Louis, and later at the Rockefeller Institute in New York. He reflects on the personalities and research of Tommy Francis, George Hirst, Jonas Salk, Albert Sabin, Wendell Stanley, and other familiar figures in virology, and on the heated debate in these years on the nature of the virus, which at the time, unlike bacteria, could not be seen microscopically nor cultured in artificial media. Assigned to Brazil in the early 1940s by the Rockefeller Foundation's International Health Division (IHD), Dr. Lennette recounts the trials and satisfactions of field and laboratory work on yellow fever and encephalitis.

In 1944 the IHD sent him to the Rockefeller Foundation Laboratories at the California Department of Public Health in Berkeley where he worked on hepatitis and set up a viral diagnostic laboratory, the first of its type in the United States. There he continued to work on encephalitis "to keep from losing my mind" in the unproductive field of hepatitis research. Another frustration was the year that he spent in 1946-1947 as chief of the Medical-Veterinary Division of the army's biological warfare facility at Camp Detrick, Maryland. Lured by a salary substantially higher than that of the IHD, and intending to concentrate in the promising new field of arbovirus research, he was instead inundated by bureaucratic red tape, "continually revising budgets upwards or downward, and drowning in an administrative morass." In 1947 he returned to California to become chief of the Virus Lab, enticed by the understanding that he would have a free hand to pursue whatever research he wished. The promise, as the reader will find, was honored throughout the thirty-one years Dr. Lennette was with the California Department of Health.

Authoritative studies on Q fever in the late 1940s and 1950s established Dr. Lennette's reputation as a physician and scientist--he possesses both an M.D. and a Ph.D.--primarily interested in clinical application rather than pure basic research. He judges the field and laboratory work with the multidisciplinary team that he assembled for these studies to be the most enjoyable of his career. By the mid-1950s Dr. Lennette and his associates had developed or refined numerous laboratory procedures for the diagnosis of viral and rickettsial diseases, and had also published on immunity and epidemiology.

\*In 1973, The California Department of Public Health was reorganized and renamed the California Department of Health. In 1978, the latter was reorganized and renamed the California Department of Health Services.

In 1954 the Virus Lab was designated a national testing center for the Salk polio vaccine field trials, which attracted worldwide attention. A highlight of the interviews is Dr. Lennette's account of his involvement in the agonizing decision to call a temporary halt to the trials in California after several deaths were attributed to the use of improperly activated vaccine. Informed of the decision, the Surgeon General's Office in Washington, D.C. immediately stopped polio vaccination nationwide.

In 1958 the National Institutes of Health awarded the laboratory a twenty-year grant to study the epidemiology and immune response of polioliike viruses. Several new viruses were discovered, and the laboratory grew in physical size and in numbers of personnel.

In the mid-sixties another large grant was awarded to the Virus Lab, this time from the National Cancer Institute, to study the role of viruses in human cancer. Not a subject of particular interest to Dr. Lennette, as he admits in the interviews, the project nonetheless led to further expansion of the laboratory.

The training programs which Dr. Lennette established remain a major vehicle for teaching diagnostic procedures in viral, rickettsial, and chlamydial diseases, a subject largely ignored in academic departments and still only taught in a few institutions. A remark in the interviews suggests the singlemindedness with which he sought to establish proper virological techniques in the medical and scientific professions. "Now in my earlier days I guess I was really expecting too much (of medical practitioners), because to me virology was practically all there was to medicine."

Over the years Dr. Lennette has also served as editor of several textbooks on diagnostic procedures for viral and microbial infections, which have become virtual bibles in the field.

In the interviews, particularly in the discussions of the interactions between the state legislature in Sacramento and the California Department of Public Health, the reader discerns the strength of Dr. Lennette's personality and opinions. With like strength Dr. Lennette directed the Virus Laboratory, wrote grant applications, and negotiated with state and federal officials. As he himself remarks, "There was no question either here in Berkeley or in Sacramento as to who ran the laboratory.

Dr. Lennette retired in 1978 with the satisfaction of finding himself and his staff internationally regarded as authorities on viral diagnosis. Such stature was to a large extent due to Dr. Lennette's firm leadership and sustained effort throughout his career to establish high standards in his specialty.

Lest retirement be equated with inactivity, let it be stated that Dr. Lennette is anything but idle. Soon after his wife's death in 1981 he became a consultant with Virion, a Swiss pharmaceutical firm seeking to establish a branch in the United States.

His responsibilities, which he describes in the final interview, require lengthy trips to Lausanne and frequent communication with the Food and Drug Administration in Washington. Dr. Lennette also is president of the California Public Health Foundation, whose purpose he outlines in the interviews, and serves as chairman of the board of trustees. In addition, he continues to attend medical and scientific meetings, and to serve as editor of the textbooks with which his name has long been associated.

Before beginning the interviews, I met with Drs. David and Evelyne Lennette, Dr. Lennette's son and daughter-in-law, who had graciously arranged for Virolab, their viral diagnostic laboratory in Berkeley, to underwrite a major portion of the interviews.\* The Lennettes, both virologists, went over the major stages in Dr. Lennette's career and pointed out significant papers in his bibliography. The Lennettes also coordinated additional donations, and advised and encouraged the project throughout the five years it was in progress.

In further preparation for the interviews, I talked with Dr. Nathalie Schmidt, a colleague of Dr. Lennette since her arrival at the Virus Lab in 1954. His collaborator for many years, she was well qualified to designate topics for discussion and to point out important papers. Dr. Schmidt died unexpectedly on July 8, 1986, before she had had an opportunity to read the interviews.

At the Lennettes' suggestion, I also met with Dr. Clara Nigg, an elderly microbiologist living in retirement in Oakland. I subsequently taped a single interview with Dr. Nigg who was one of the first women to receive a doctorate in bacteriology (1929) and to pursue a full-time career in microbiology. The transcript of the interview is deposited in The Bancroft Library.

Eight interviews were taped with Dr. Lennette between August of 1982 and February 1983. The first few sessions were conducted in Dr. Lennette's commodious office in the Viral and Rickettsial Disease Laboratory. Later interviews were conducted in his office in the California Public Health Foundation in the adjoining building. A final interview was taped in November 1986 in order to expand on research previously discussed, to take proper note of the recent death of his long-time colleague, Nathalie Schmidt, and to describe Dr. Lennette's current activities on behalf of Virion.

\* Virolab is currently underwriting interviews with Harald N. Johnson, another physician-virologist associated with the Rockefeller Foundation and the California Department of Public Health.

Dr. Lennette, a small man with a friendly manner, spoke at length and with good recall of the associates and events of his career. His pride in establishing the Virus Lab as a premier institution in diagnostic virology underlies the interviews and at times was openly expressed. We talked very little of his family and extracurricular activities, for virology appears to be the engrossing focus of his life. Heavy professional responsibilities and frequent travel leave little time for other activities.

The interviews were lightly edited and delivered to Dr. Lennette who painstakingly reviewed them and made substantial additions to and refinements of his original statements. These additions are noted in the text. Wishing to provide further information, particularly about his family, Dr. Lennette then wrote the section which appears as Addendum II in this volume. A certain amount of repetition is inevitable in a project which extended over a five-year period. The result, however, is a thorough documentation of a career in viral diagnosis and research, and of the history of the Virus Lab which he describes with justifiable pride, as "the finest (viral) diagnostic laboratory in the country."

Sally Hughes, Ph.D  
Editor, Medical History

September 1987  
Regional Oral History Office  
The Bancroft Library  
University of California, Berkeley

BIOGRAPHICAL INFORMATION

(Please print or write clearly)

Your full name Edwin Herman Lennette

Date of birth Sept. 11, 1908 Place of birth Pittsburgh, PA

Father's full name John Lennette

Birthplace Austria

Occupation Attorney

Mother's full name Natalie Frances LeManek

Birthplace Poland

Occupation Housewife

Where did you grow up ? Pittsburgh, PA

Present community Oakland CA

Education B.S., U. of Chicago, 1931; Ph.D. U. of Chicago, 1935;

M.D., Rush Medical College of the U. of Chicago, 1936

Occupation(s) Laboratory, clinical and field research on viral and

rickettsial infections of man

Special interests or activities \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

## I FAMILY BACKGROUND AND EDUCATION

[Interview 1: August 13, 1982]##

Grandparents and Parents

Hughes: Could you tell me the names of your grandparents and where they came from?

Lennette: No, I don't know much about my grandparents on either side. My mother and father immigrated to this country in the eighties or nineties. My mother, Natalie Francis Lemanek Lennette, came from a part of Poland known as Galicia, French background, and my father, John Lennette, came from Austria. Now, they were married at a very young age. My mother was about nineteen, judging by the records that I've seen, and they were divorced shortly after that. I saw very little of my father, so I don't know very much about the background of the family.

Hughes: Do you know what your father did for a living?

Lennette: Originally there were three men in the family who worked with my grandfather: his two sons, one of whom was my father, an uncle, and a man who was married into the family. The three of them worked in a firm operated by my grandfather, which in those days, I guess, was a lucrative operation, namely dealing with immigration law and getting immigrants into the country, smoothing their path with immigration law and bringing in their money and their possessions and setting them up in this country in areas of employment or with friends or relatives.

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##This symbol indicates that a tape or a segment of a tape has begun or ended. For a guide to the tapes see page 319a.

Hughes: But they weren't actually lawyers.

Lennette: No, they would be what today you would call paralegals. That term didn't exist then. The firm did very well, I guess. When my father and mother parted company--not too many years after they were married--I lost contact with him and never knew him very well because I lived with my mother. After the big wave of immigration sort of subsided there wasn't much of a business left, I guess.

I don't know what my paternal grandfather, Bernard Lennette, did, but for years he had an office in downtown Pittsburgh, Pennsylvania, where I was born. And my father, about whom I would hear only occasionally, had various positions. At one time he was with the commissary department of different railroads. He even was a steward at one time, I guess, just to see what this job was all about. And that's about all I know about him.

Hughes: You didn't see him while you were growing up?

Lennette: No, I grew up without a father. There have been only two women in my life: my mother and my wife.

Hughes: Did your mother have to work for a living then?

Lennette: She had to work for a living. I guess she was just in her early twenties when they were divorced, so most of her life she had to work to support me and my sister, Henrietta. There were three of us actually, two girls and a boy. I was the oldest and I had a sister two years my junior. Another sister died in infancy, so I never knew her. My sister, Henrietta, who lived in Pittsburgh all her life, just died recently, in 1979. So there were just the two of us, and my mother brought us up, worked at a variety of jobs and did very well, and then she died very young, thirty-eight, of cancer.

Hughes: Was it a struggle financially?

Lennette: For her?

Hughes: For all of you.

Lennette: It was for her because in those days women didn't have the positions or the opportunities they have today, so she had to do whatever was available, I think, including a job as a cook in one of the hotels, a chef, a sort of supervisor. And there were times when things were a little bit tight. We never starved. We never lacked for food or clothing, but we didn't have any--what do they call it--discretionary money, that's what they would call it today.

Lennette: But I didn't know the difference; I didn't know what it was to have that kind of fun, because the community, the neighborhood, in which I grew up was not a very wealthy community. I mention this because most people think that M.D.s come from an illustrious background with lots of money to put them through medical school. That isn't so. My medical school contemporaries, or most of them, were hard-working people with no money. I'll tell you about that a little bit later.

Hughes: Was it an ethnic neighborhood?

Lennette: Yes, pretty much. There were Germans, Poles, Ukrainians, Russians, a fair number of Italians; they were all sprinkled around. It was on the south side of Pittsburgh. It was an industrial area with a concentration of steel mills.

Hughes: Did you speak English at home?

Lennette: Yes. And French and German. As a matter of fact, I spoke French and German before I spoke English, because my mother was insistent--well, my grandfather was, too--that we have another language. But once you get with the rest of the kids, you don't want to be different. You just turn everything off, so I forgot most of it.

Hughes: Lennette doesn't sound very Austrian to me.

Lennette: It's French.

#### Grammar School and High School

Hughes: Where did you go to grammar school?

Lennette: I went to grammar school at the so-called Humboldt School on the south side of Pittsburgh.

Hughes: Do you have any particular memories of those years?

Lennette: Yes, I had a couple or three very fine teachers. You look at me and say I am kind of a fair-looking individual. I was never very big--I'm small-boned--so I avoided all sorts of violence with students and bullies and I guess it was sort of a reaction, avoiding all this violence, because I probably couldn't hold up my end. I did a great deal of reading, so I spent a lot of time at the Carnegie Library. Libraries were a relatively new phenomenon back in the twenties, right after the war. I got a pretty good background in literature and learned how to use the English language effectively and developed a love for good usage and expression.

- Hughes: You were concentrating on the humanities more than the sciences at this stage?
- Lennette: Yes, I was a voracious reader. I still am. I have more books than I could possibly read. I've been saving them all for retirement, So I have to get to them. Plane rides are the only time I have today. But the librarians all got to know me pretty well, so they knew my taste and what I was trying to accomplish.
- Hughes: Did your mother encourage you?
- Lennette: Yes, she did, very much so.
- Hughes: So education was important to her, too.
- Lennette: Yes.
- Hughes: What about your sister, was she encouraged as well?
- Lennette: She was, but, you know, women's outlook in the twenties was quite different from what it is today. Her main focus, I think, was on getting married. She did marry at about age eighteen or nineteen.
- Hughes: So she didn't go to college.
- Lennette: No. She had no interest in that.
- Hughes: You mentioned that there were just two women in your life. Was there anybody else outstanding in your growing up years outside the family that may have had an influence on you?
- Lennette: Well, not in terms of closeness. I was very close to my mother, very close. I adored her, because of what she was trying to do for us two children. Then I married my childhood sweetheart. There was never another woman. We'd been married over fifty years when she died, just a year ago. [1981] So those were the two women in my life.

But there were other women who had, yes, a decided impact on my education and future. I remember one teacher in mathematics who gave me a hard time. That was in high school. But she got me straightened out in math. I didn't know what it was all about, and I've thanked her ever since. I had another one, a male, who was a physics teacher. He gave me sort of a liking for science, which was one of my first exposures, in high school. And the third teacher, who perhaps had the greatest impact, was my English literature and English language teacher, Anne Campbell. I still remember her. She was the one who imbued me with a love for the English language, that there are more than a half a dozen words that you can use, that there is a massive vocabulary that people can acquire if they want to look at the dictionary and use it properly. There are nuances which are expressed by antonyms and by synonyms, and why not use them.



*Upper Left:* On the right, Dr. Lennette's mother, Natalie Francis Lemanek Lennette, on her wedding day, 1907.

*Bottom:* First row, EHL, fourth from right, 6th or 7th grade, Humboldt School, Pittsburg





Hughes: This was in high school?

Lennette: Yes.

Hughes: By then you had quite a bit of reading under your belt to draw upon, I imagine.

Lennette: Yes, I did. It just came to me naturally, and I spent a fair amount of time with books. I was always very conscientious about homework. I was never a problem child. And this didn't give me any trouble with my peers, because many of them came to me with their own problems, for example, to help write a letter applying for a job. You see, they couldn't quite phrase it. "Well, we'll get this guy Ed who knows..." So I ended up writing their letters. I can still remember that. Then later on in the university I had another mentor in the science field. [see below] He, too, inculcated in me a love for the English language.

Hughes: Good, not all scientists have that.

Lennette: No, but it has its drawbacks, because I became furious at some of the things I read, and to think that somebody with a university background should write as poorly or be so slovenly in his presentation. Well, the reason for that is--I don't know how relevant this is here--lack of a classical education. These people have a high technology education. They are not exposed to literature or languages or paleontology or whatever. They're just in a very narrow field. When I was teaching here thirty years ago, twenty-five years ago, you had to define the words you were using, whereas if you had any Latin or Greek they would come to you automatically--you knew the etymology, you knew the roots.

I was amazed at the ignorance of these people when it came to Latin and Greek. Most of them never had any. I had a year of Greek and three years of Latin, and I thought that wasn't too bad. Well, at the time I was doing it, I wasn't too happy about the Latin part; the Greek was interesting. But in retrospect I'm glad they made me do it.

Hughes: What was the name of the high school?

Lennette: South High. It was a high school that drew on a large neighborhood, because we had some outlying boroughs which didn't have their own high schools. Well, the same exists here. The city councils would send their students to the closest high school and pay their tuition. So we had a lot of students who didn't come from that immediate area, including some who came from very wealthy neighborhoods, neighborhoods which subsequently developed their own high schools.

Hughes: Did it have a reputation for being good academically?

Lennette: No. The really good high school at that time--I went to South High, which is right in the middle of a mill town really, the whole city is a mill--the really good high school with status was Schenley High School, named after the Schenley family. That was way out on Fifth Avenue, right in a very posh area. very wealthy people. It had a good reputation for academic studies.

Hughes: You mentioned a physics teacher. Was there any exposure to the biological sciences in high school?

Lennette: Yes. I forgot the first name; oh yes, Alice Lord was her name. She was a big woman, as was Anne Campbell. Mrs. Lord was a very good biologist, and she used to take her students out on field trips. A lot of these kids didn't care whether school kept going or not, but some of us were really interested, and with those of us who were interested, she took extra pains. We didn't have to go too far out of Pittsburgh in those days to get out in the countryside, where she would point out snakes and various other forms of life that she would uncover under the rocks and so on. She was probably in one of the first ranks of ecologists. They didn't call them that in those days; they were just zoology teachers. She was right in the ecology group. And a very fine woman.

Hughes: Were you thinking about what you eventually wanted to do?

Lennette: Oh yes, I wanted to go to medical school.

Hughes: Why?

Lennette: I don't know. I suppose a lot of the reading about the time of the Romans on into the Renaissance, and so on, and exposure to the classics of science and medicine, like Vesalius, for example, and Harvey and some of the other early physicians, gave me... I didn't know whether I would like the practice of medicine. I just decided I wanted to do it. Of course later on I got side-tracked.

Hughes: We'll talk about that.

Lennette: But I did have that desire early on.

Hughes: Beginning with high school?

Lennette: Yes.

Hughes: What about extracurricular activities aside from reading? Did you have a job or any particular hobbies?

Lennette: Yes. Being small as I am, and opposed to violence in any form, I wasn't about to become a football player, so I became manager of the football team. [laughter] That was extracurricular.

So that gave me a big S to wear on my sweater, which was de rigeur. The other was I became editor of the high school--not the class book--but we used to have a periodical that came out occasionally, maybe once a year or twice a year, and I was editor of that. I was also editor of the class book.

Hughes: Did you ever have any after-school jobs?

Lennette: Yes, I worked in a pharmacy close to the high school. In those days we used to walk; we didn't ride buses. We didn't have bus fare to begin with. You walked twenty, thirty blocks. It was nothing to walk a couple or three miles; nobody thought anything of it. So we'd walk, and the job was close by. And I got the munificent sum of fifty cents an evening, from six to twelve.

Hughes: Assisting a pharmacist?

Lennette: Yes, I did everything. I, amongst the other things, would mop the floor, run the soda fountain, rearrange the shelves, unpack materials and put them on the shelves.

Hughes: Did you learn anything that you could use later?

Lennette: Yes, because when things were slow we'd sit down and talk. Two brothers ran the pharmacy. This is back in the days of Prohibition, so I guess a fair amount of alcohol was sold, too, sub rosa. So I learned something about pharmacy from these people, and drugs. Fifty cents a night, that doesn't sound like much, but that fifty cents was very helpful. That went a long way. That's in the days of penny candy, you know.

Hughes: What about your decision to go to college? Why the University of Chicago?

#### The University of Chicago, 1927-1936

Lennette: The University of Chicago had always had a good reputation. It was a new school, relatively speaking. It dated only from the 1880s, 1890s, and John D. Rockefeller had poured a lot of money into it. He was a founder and actually built the school, and he got the finest scholars he could find, like its first president, William Rainey Harper. Not so much in the sciences, but in the classics. He brought together a tremendous faculty, and people just had to respect that school, because it was good competition for the classic schools back East--Harvard, Yale, Princeton. Everybody had heard of it who had any exposure. This came a little bit later.

Lennette: On top of that, I knew that they had a good medical school in Chicago by the name of Rush Medical College, affiliated with the University of Chicago, and that's where I wanted to go. The University of Chicago had a medical school, but it was only the first two years, the preclinical years, which were physiology and chemistry, bacteriology and so on, and the second two years, the clinical years, were done on the west side of town--that's where Rush was. Rush was a school that was founded many years before, actually in 1837, its charter antedating that of the University of Chicago by two days! I think Rush was originally tied in with one of the smaller colleges in the area--the name escapes me. Anyway, the University of Chicago affiliated with it to provide training in the clinical field. It had a very good reputation for its practical clinical training; it was not a research-oriented school. The main thrust was all practical work, practical surgery, practical medicine, practical OB [obstetrics]. So I thought that's the place for me.

Well, how do we do this? My mother died in 1926. She was ill. She was born in 1888, so she was thirty-eight when she died and left us two children adrift. So my sister went to live with my grandfather's housekeeper. He had died a few years before, and the housekeeper was living close by.

Hughes: You were just finishing up high school, then, when she died?

Lennette: I had just finished high school in 1925. I wasn't quite seventeen. So I spent a little time at the University of Pittsburgh. I worked at night in a steel mill, a position which I got through my uncle, who was a personnel director. It was supposed to be a summer job, and then it went on into the fall. It was a pretty good situation, because I started on the job at about eight o'clock in the evening, seven o'clock, weighing bar metal used for the production of wrought iron pipe, and was through about one or two in the morning, so I could go home and get some rest before I went to classes. It was all right. I was young enough; I could take it. I was only seventeen, eighteen. This worked out quite well. This was the year that my mother was so ill and was going downhill.

So at the end of the year, 1926, she had died, and I had three aunts living in Chicago, two married, one single--beautiful women. The latter decided I ought to be in Chicago with the rest of the family, where I would know somebody. I didn't have any relatives in the Pittsburgh area. Well, I did; I had an uncle who was a personnel man for the mill. So I said okay, I'll go to Chicago. They've got a good school there. Because of finances, I applied to the University of Illinois, but was turned down, because I had to take some remedial courses to make up deficits! I said, well who needs that? I applied to the University of Chicago, academically a far better university, with no idea I'd be accepted there. I was. So my

Lennette: whole career in higher education was at the University of Chicago. I did my undergraduate work there, my graduate work and also all my medical work. So I spent about nine years altogether during the course of the studies.

Well, anyway, I went to Chicago and lived with one aunt while I was going to school. That was a long commute from the north side to the south side by elevated train. My father was paying part of the living expenses. I never saw him. This was all told to me by my aunt. He was rather erratic about all of this, too, because sometimes money came, sometimes it didn't, and he had a family to support also. I think the family was living in Denver. So you can't fault him on that. This is now 1927.

Hughes: The Depression.

Lennette: Was coming, yes. In the meantime, the girl to whom I was later to be married had had her training in Pittsburgh also, Frick Teachers' Training College. She was a schoolteacher, but never taught any school. She just went to New York and had a very good position there. She was a secretary to a buyer for a glove house and made a little extra money by posing as a glove model. All you ever saw were her hands. She had beautiful hands. And always one hand without a glove, and the other one pulling the glove on. So during her summer vacation that year, it was July or August, she came to Chicago, looked for a position so we could be together. Couldn't find one; she went back to New York. And I ended up in New York in the fall of that year--this was '28. I thought I might as well be somewhere where I had somebody whom I knew, and we were going to make our future together. So I went there and I worked for General Chemical Company in the accounting department. Hated every day of it. That was not my bag, as they say.

Hughes: Had you started at the University of Chicago at this stage?

Lennette: Yes, I had one year, from '26 to '27. Then my youngest aunt came to my mother's funeral. She was about ten years older than I, as I say, a beautiful woman, a stunning woman. She decided I ought to go back to Chicago with her. I said no way would I go. Later on I did, but on my own. So I ended up living with one of my aunts for that year, and it was a little bit difficult financially, because things were getting tough. The Depression was just beginning. So then I decided I shouldn't inflict any further hardships on the family; I ought to get a job somewhere, and so I went to New York and spent the next two years there. I also wanted to earn some money so I could come back to Chicago and continue my undergraduate education.

My fiancee, Elizabeth Hubenthal, had a room in New York. She stayed at Laura Spelman Hall.

Lennette: It was a girls' dormitory. She lived there with a lot of other working girls. Spelman was the maiden name of one of the Rockefeller family. And I had a room on the East Side, about 86th Street. That was a long ride all the way down to Rector Street, in the financial district, but I couldn't afford anything else. So I worked there for two years and salted away as much money as I could. She put some away, as much as she could. And then in the fall of '29 I decided I had enough funds to go back to the University of Chicago, at least for another year.

I got back in early September or late August of that year, and as you know, came Black Friday in October, I think it was, the market crashed in '29. Elizabeth came out to Chicago that spring, I think. She lived over on Kenwood Avenue, as I recall it. People don't know what these apartments were like anymore. She had a one-room apartment, plus a little kitchen. There was a Murphy bed in the wall that you pulled out.

I had an apartment close by, similarly a very small one, very tight. So I started back in school as a junior in '29, and then we decided, well, why all this expenditure of funds, we might just as well get married. Now, had that been 1970 there wouldn't have been any problems. But the mores of that time were quite different from what they are today. That was a money-saving move, essentially. So through all of this struggle through school she was my partner. We worked together all the way through medical school. This is why I just don't have much patience or sympathy for these people who marry and allow their wives to work and get them through law school or dental school or vet school or medical school, and then just brush them aside. I think that's totally unforgivable. Women shouldn't be used that way.

Hughes: Had you chosen a major at this stage?

Lennette: Three of them. I started out in chemistry. I got as far as physical chemistry and I couldn't make it--I didn't have enough math--so I had to back off and try zoology. And I didn't like that, so I went into bacteriology, which was microbiology actually.

Hughes: So it was almost by a process of elimination?

Lennette: Yes. Something that would fit my intelligence. So I got into microbiology. At that time it was called bacteriology; microbiology didn't exist per se. This was the department of bacteriology and hygiene.

One of the instructors, who was an associate professor, I guess, was a great big man by the name of Gail Monroe Dack. This was 1929. He had gotten his Ph.D. in bacteriology about three years before and was now enrolled in medical school. He didn't think that these



Edwin H. Lennette, graduation, South High  
School, Pittsburgh, 1927



Dr. Lennette's Wife,  
Elizabeth Hubenthal Lennette  
at about age 18



Lennette: dumb students were learning enough bacteriology to practice medicine, so he was riding us pretty hard. It wasn't like it is today; you didn't talk back to your teachers; you bowed and scraped. So when he would walk into the room, all the students would leave by the other door. They were scared to death of this big guy, who was very bluff and straightforward speaking, gruff. Maybe even a little bit rough. And I always stayed out of his way. Why ask for trouble?

One day he let it be known that he wanted to see me in his office. I said, "Well, Jesus, here we go. I guess I won't make it." So I went into his office. He said, "How much money you got left?" I didn't know what he was talking about. I said, "Well, why? What?" He said, "I understand you are saving your money to come back to the university." I don't know where he learned all this. He said, "How much you got left?" I said, "About three hundred bucks." This was now almost Christmas. I had another two quarters to go. Of course, it wasn't much. The tuition, I think, was fifty or seventy dollars a quarter. Well, he didn't think that was enough. He asked me if I wanted a job. I said sure I'd like to have a job. I'd been washing dishes over in the botany department, all these terrible Petri dishes with all these stinking fungi in them. I was getting fifty cents an hour or something like that. Sure I wanted a job. "Would you like to be a teaching assistant?" I said sure. So he gave me a job as a teaching assistant.

Hughes: Do you think he had singled you out because he suspected that there was some promise there?

Lennette: I'm not sure. All I can say is that all this gruffness was exterior; underneath all this fear and panic he put into the class he was just a soft-hearted individual. So it came down to, he was really concerned about me. So I said, "Sure, I'd love to have the job." This may be out of sequence, but a sequel to that is that I had that teaching job all year--this was till 1930--and then somebody was supposed to teach a course in public health, bacteriology.

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I didn't know what this was all about. So anyway, Bob Crawford, who has since become a very prominent orthopedic surgeon, was taking bacteriology. He was working under Edwin Oakes Jordan, a very famous, internationally-renowned microbiologist. So Bob and I taught this course. It was three months, a whole quarter. That was good experience.

The next year was 1930. They got another faculty member, real tall, statuesque redhead. Quite a gal. Beth Verder was her name. She was to teach this course, and she was also teaching pathogenic bacteriology. Gail Dack came from a farm in Illinois, and she came from a farm in Iowa. She was not a backwoods person. She had been around. She knew what the big lights were like.

Lennette: This was early 1930, and just about exam time we had this tremendous blizzard in Chicago. I came and looked out the door, and you couldn't find the steps. We lived in a row of brownstone houses with all these high steps. Just everything was covered, so I couldn't make the exams. Finally they gave the exam. We got there and I was just as sick as I could be. Beth Verder saw that I was in trouble, and she asked me what was wrong. I told her I just didn't feel very well. She said, "You don't look well. You look like you have a fever, and you're probably coming down with influenza"--which I was--"you better go home." I said, "I'll take this exam." She said, "You take it some other time." She let several of us go home. I never forgot that episode, because here was somebody who really cared about the students. It wasn't like this place up here [University of California, Berkeley] which gives rise to Mario Savios. So she and I and my wife have been friends all these years. Beth's still alive, living in Washington, D.C. She's a little over 80.

Hughes: That was unusual to have a woman in an academic position, particularly in bacteriology, in those days, was it not?

Lennette: Yes. She was an instructor, and a good one. A very good one. And then we had a couple of research women who didn't do much teaching, but were carrying out research projects. One worked on diphtheria and one on streptococci. We didn't have all these rules and regulations to bother us that have since grown up.

Hughes: Did you do any research as an undergraduate?

Lennette: I participated in some. Times were tough; you needed money to get by. Gail Dack was working on staphylococcal toxin food poisoning. This is history now, and is known and taken as accepted fact. At that time they knew about botulism, and they thought that the staphylococcus was probably also involved in food poisoning, because it produced a toxin which when inoculated into monkeys gave them vomiting and diarrhea and the staggers, as it were. We had to find out what this did to man. So one of the ways of doing this was to bake a cake and mix up the batter and put the bacterial culture into the batter, or else put it into the custard between the layers, and everybody have a piece of the cake. Well, we did this several times, and of course, we got the usual reactions to the toxin.

So the next thing was to get this toxin out, as I remember. So they got the toxin separated from the bacteria, and they tried to purify it. Then they heated it for different intervals of time, two minutes, five minutes, ten minutes, twenty minutes, half hour. And each of the volunteers, so-called, in the department would quaff a bit of the stuff. Well, I got the stuff which had been boiled a half an hour. And I thought, "Gee, I've got it made." I never made it across the Midway Plaisance. There was a huge

Lennette: plaisance, a depressed area, between 57th and 59th Streets. That's where the old World's Fair was, all along that strip. It's a beautiful strip. It's all lawn. I got about halfway across, and it really hit me. I was vomiting. I had diarrhea. Sometimes both at the same time. I never made it back to my room.

Hughes: It takes about half an hour to...

Lennette: Yes, it just hits you like that [strikes the palm of his hand with his fist] all of a sudden. And so this is the way we made a little side money. Once in a while we'd go down to St. Luke's or one of the other hospitals and give a little blood for transfusion. This is what you needed for income.

And this is why I become annoyed at students who complain about the fact that they are not getting their GI Bill of Rights and that they're not getting adequate funding. They don't know what it is to have to shift for themselves. Nobody cares whether you go to college or not. You're on your own. You want to go? Make it on your own. Get enough interest, you can do it. That's what I tell all these kids. Even my own children.

#### Virology Instruction in the Thirties

Hughes: Were you told anything about viruses in your undergraduate courses?

Lennette: We had in my senior year a course in virology. Virology was essentially an unknown field. The course was given during the summer of 1930 by Professor Earl Baldwin McKinley. He was dean of George Washington University Medical School in Washington, D.C. McKinley came out that summer--the summer of 1930--to teach this special course in virology, and brought with him his assistant, who did all the menial things like inoculating rabbits, shaving their ears or whatever, plucking the hairs out of the guinea pig belly. She was a real knowledgeable assistant. I took to her. We didn't even have a textbook. The only text we had was a collection of reprints out of the Philippine Journal of Sciences. One was on smallpox; one on molluscum contagiosum. Another one was on smallpox. One on yellow fever; not much was known about yellow fever. And this was our text.

Hughes: [Thomas] Rivers' book was...

Lennette: Wasn't even out. He had a book in 1927. But it was not a text. It was a collection of lectures or essays which he gave at Stanford. They're beautiful lectures, but it was not a text. Well, neither was the stuff that McKinley was using. These were just reprints of articles he had written, but they were sort of textual in the sense that they were summaries of the current status of the field.

Lennette: This was 1930. Yellow fever virus had just been discovered in 1927, in Africa. The Rockefeller Foundation had a big laboratory in West Africa, in Lagos, Nigeria. And on the staff was a chap by the name of Johannes Bauer. Johannes Bauer was a staff member of the International Health Division of the Rockefeller Foundation, a Swede who had done a big job in Europe right after the war in trying to get people settled and fed. And quite a tyrant in his own way around the lab, as I had reason to know, because I worked for him later on and I knew him personally. Another member of the yellow fever triad was a Britisher, Adrian Stokes. Adrian was sort of the chief of staff, as it were. And the third was N. for Noel Paul Hudson. That's the three. They wrote this paper on the isolation of yellow fever virus. And in retrospect it was obvious that their approach should have been made a long time ago. They didn't use the local monkeys. They got monkeys in from India, where yellow fever doesn't occur, and these monkeys were found to be susceptible. All the animals they were testing locally had probably had yellow fever virus infections, so nothing would take. And the blood specimens that they used for isolation of this virus came from a native by the name of Asibi. Asibi is the classic strain, not the classical, the classic strain of yellow fever virus.

Shortly thereafter Hudson decided he would take an academic position. He had attended Harvard Medical School, as I recall, and he also had been on the staff of the Mallory Institute, which is an institute of pathology associated with Harvard and the other medical schools in the Boston area. So he came to the University of Chicago as the first professor of virology.

Hughes: Of virology?

Lennette: Of virology. Not bacteriology.

Hughes: That's interesting.

Lennette: Now, if you wanted to learn virology at that time, there weren't very many places you could go. You could go to the Rockefeller Institute, where you had Tom Rivers teaching. Rivers was a pediatrician by training, but he was teaching virology and doing virology. He was an authority. Or you could go up to Columbia where there was a chap by the name of Claus W. Jungeblut. Or you could go to the University of Wisconsin, where they had a chap by the name of Paul F. Clark, who was teaching in the department of bacteriology. He was better known as "Fishkettle" Clark, because he put all of his dirty glassware into these fishkettles for sterilization. Or you could come out here to Stanford, where there was Edwin Weston Schultz. And that's about it.

Hughes: How about [Karl F.] Meyer?

Lennette: Meyer was not doing any virology at that point. He was deeply immersed in plague and tularemia. Later on he got into psittacosis. Psittacosis is not a virus. It was thought to be a virus in those days, but it's not a virus. So he didn't get into virology until somewhat later.

#### Paul Hudson's Yellow Fever Research

Lennette: So here we have this professor, Hudson. He arrives on the scene at the University of Chicago, Ricketts Laboratory North, with all these boxes coming in from Africa and from Boston. Gail Dack gave me the job--I don't know, fifty cents an hour or something--to unpack all these boxes and put everything up on shelves--lots of books, a lot of little mason jars and little stopper jars with wax seals on them labeled Noguchi. Well, Hudson had done the autopsy of [Hideyo] Noguchi, and he had some of Noguchi's tissues there just in case of future questions or disputes. Of course, you couldn't do that today because of all this business, often ridiculous, of informed consent. You've got to get ninety-seven people to sign before you can throw away the appendix. But he had all these tissues which were used to show that Noguchi actually died of yellow fever.

You hear a lot of stories about Noguchi. He was really maligned because he was not the discoverer of yellow fever virus. He was working with a spirochete. But that wasn't his fault. He was a Ph.D. and he was getting material in New York; it was shipped up from Latin America. And the diagnoses were entirely clinical diagnoses. What these people were dealing with was not yellow fever. It was a wild disease caused by Leptospira icterohemorrhagiae. So Noguchi in good faith thought he was getting this spirochete out of yellow fever material. Well, when he realized that things weren't going right, he tried to justify some of the things he was doing, and just got himself involved more and more deeply.

Hughes: That must have held up the discovery of the actual virus, though, when you have a man with the prestige of a Noguchi saying it's a bacterial cause.

Lennette: That's right.

Hughes: How do you suppose that the team, Hudson and...?

Lennette: I think the team was set up partly to answer that.

Hughes: Were people thinking it could be a virus?

Lennette: Yes.

Hughes: Had they done the usual filtration studies?

Lennette: Yes, but they were not getting consistent diagnoses. It was only when they got a field station in the heart of yellow fever country, and brought in patients like Asibi, who had all the classic symptoms of yellow fever--black vomit, fever, aches, pains, nausea, jaundiced eyes and so on--that one could make the clinical diagnosis. Of course, it's hard to tell with a Negro whether he has jaundice. Then you get a virus out; there must be a cause and effect relationship. And the first virus out was Asibi's. That station was set up in West Africa just to answer some of these questions. I think the virus was actually found about 1927.

Hughes: Yes, 1927.

Lennette: My memory's still not too bad.

Hughes: According to Rivers, there was an epidemic at that stage, too, which was some of the motivation for sending out the three-man team.\*

Lennette: There were more people than that. There were about five or six people.

If you go to Ghana, to Accra--that's where the laboratory actually was--you'll see a bust of Noguchi, who died there. There's a typical little Japanese garden around it with a small fence. He was very highly regarded and respected, and nobody started tearing it down because he was wrong.

Hughes: Because Noguchi's background was pretty strict bacteriology, as far as I'm aware, do you think he would have had the mind set to even look for a virus?

Lennette: I can't answer that except to say that virology was in a very infantile stage at that time. People weren't oriented towards looking for viruses and trying to diagnose viral diseases, because the prevailing attitude was if you rule out all the bacteria and you can't find anything, you throw it to a wastebasket labelled "viral disease." It doesn't tell you what; it's just a viral disease. We did that with many diseases but eventually we worked them out.

Hughes: Did Paul Hudson have any particular background that would predispose him towards virology?

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\*Tom Rivers: Reflections on a Life in Medicine and Science. An oral history memoir prepared by Saul Benison, Cambridge, Massachusetts: MIT Press, 1967, p. 97.

- Lennette: No, he was the junior member of the team, and he was trained as a pathologist, so he was doing all the liver examinations.
- Hughes: There must have been somebody on the team, though, that had some exposure to virology.
- Lennette: Stokes had some exposure to virology, yes. And Johannes, I think-- I may be wrong--was a clinician in large part, but also an experimental pathologist.

Virology Instruction in the Thirties (continued)

- Hughes: Let's get back to the course that you took that summer. Can you remember how it was approached?
- Lennette: There was a series of lectures, I think three a week, and they were very good.
- Hughes: Disease-oriented?
- Lennette: Disease-oriented, yes.
- Hughes: Was there any discussion of the possible nature of the virus itself?
- Lennette: Yes, there was some, but there really wasn't very much known, and the speculation that went on--well, part of it's been proved today, because what they thought was that the virus most probably represented a gene, either a piece of a gene which had been broken off from the rest of the genetic material of the cell and then became a free-living virus, or was introduced from somewhere else. Most probably the former; it was probably a piece of the genetic material broken off.

Well, over the years we've found out that viruses are probably related to the genes of the cell, as witness the oncogenes, and then become free-living on their own, because when you get right down to it, what is a virus--just a little piece of RNA or DNA surrounded by a protein coat. You can't get anything simpler than that. Once you take off that coat, the thing generally dies. So it could very well just be genetic material.

The first real textbook, if you want to call it that, on virology was produced by [Clennel E.] Van Rooyen and [A.J.] Rhodes, a great big volume. It's called Viral Diseases of Man.\* I have both editions at home.

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\*Viral Diseases of Man, London: Oxford University Press, 1940 and 1948.

Lennette: Van Rooyen's up in Canada now at Dalhousie University. Van Rooyen, when I saw him about two years ago, said that after the 1948 (2nd) edition, he'd never put out another edition. He said he just was working full time filling cards like yours with all the information that he would have to put into a new book. He said, "I'm forever revising it." So he gave up on it. But those were two monumental works. And if you want to know what virology was like prior to the appearance of these two books, you'll get a very good picture from them, because it's beautifully presented, and in some detail.

Hughes: That's interesting that by the summer of 1930, people were really talking about viruses in terms of genetic material rather than just a very minute microorganism, which, when you read Rivers' early papers, is his prediction.\* A lot of his contemporaries even thought that obligate parasitism could be explained away by the statement that we just haven't found the proper culture medium yet, but it will come.

Lennette: Well, that's been true in large part; we probably just haven't found the right growing conditions.

Now when Hudson got to Chicago--he's a very good friend of mine now; I call him periodically; he's retired, living in Florida--all these crates and boxes had been unpacked and everything stacked up in the laboratory on the shelves, and the animal house was cleaned. Gail Dack brought me in to see Hudson. He said, "You're going to need somebody to help you in the lab. Here's an assistant for you." And Hudson looked at me: "He's too scrawny. He can't catch any monkeys." I only weighed about a hundred and twenty pounds at that time. Dack said, "Well, how do you know? You're not much bigger yourself. Are you going to catch them?" Anyway, he prevailed upon Hudson to give me the job catching monkeys and helping out in the lab.

Hudson had eight graduate students, including me.\*\* Some of them earned their degrees over the next several years and left for teaching positions. Jim Harrison ran out of money, so he went back to his native Texas to teach. Francis Gordon developed tuberculosis and

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\*See for example, T.M. Rivers, "Some general aspects of filterable viruses," in Filterable Viruses, edited by T.M. Rivers, pp. 3-52. London: Bailliere, Tindell and Cox, 1928.

\*\*Floyd Markham, Oram Woolpert, Francis Gordon, James Harrison, Joseph Stritar, Edith -----?, Irving Nieman.

Lennette: ended up here in Martinez at a sanitarium for several years until he recovered. Martinez at that time was the place to go for TB therapy, believe it or not. This was back in the early thirties, but you wouldn't go there now with all those refinery fumes and degraded environment.

So this sort of disrupted the whole group. Nobody left except Lennette, our monkey catcher and major factotum in the lab. We had a big grant (I think we had five hundred dollars) to work on polio, which came from the Milbank Fund, so Hudson came in one day and said, "We lost our crew here. We've got to continue this research, and I can't do all this alone. I've got to teach." (He had many other obligations too.) "Why don't you work for a Ph.D. in bacteriology?"

Hughes: This was before you even had your B.S.?

Lennette: Yes, I was a senior in college ready to go to medical school. I'd been accepted by the University of Chicago Medical School, and now he was giving me this line of approach to a graduate degree. It kind of shocked me. I said, "I don't think I'm interested, but if there's a bit of money involved I might consider it." You know, forever pecuniary reasons. He said, "Oh, we can get you a stipend." It didn't turn out to be very much, but it would be of help. So I gave it some thought and I talked it over with Elizabeth, my wife. She said, "Sure, if this is what you want to do, go ahead." She never stood in my way on any of these career things, even if it entailed more obligations. She always let me do as I wished. So I decided I'd work for a Ph.D.; it couldn't be too bad.

The result was, I went to classes all year round. All I had was September off, and then I worked that month around the lab, because all the grad students would take off, so I would have a schedule of whose rabbits were out in the animal house there, whose guinea pigs or mice, and what to do with them. I'd go out feeding rabbits here, sacrificing mice there, and made myself a fair piece of money during the September interlude. The other four quarters, including the summer quarter, I was taking classes. Now, if I was registered in the graduate school I payed seventy dollars a quarter; if I was a graduate in the medical school so I could get medical credit for the course--it would be the same course, you see--I had to pay ninety dollars to get those credits. So I was sort of alternating these courses. I was doing both at the same time. And working for Hudson.

He was quite a person. I used to do a lot of dogsitting for him. He never had any children of his own. He and his wife, Emily, later adopted two. They had a dog they were very fond of, so I used to dogsit for them.

Hughes: So you were becoming a friend.

Lennette: Oh yes, we became very good friends, but for years I never addressed him by his first name, not until recently when he insisted I do so.

Well, what happened in 1939--we had already gotten our degrees--there was a big international congress of microbiology in New York. At this meeting was N. Paul Hudson, as a virologist, and one of his colleagues, Paul Cannon, who was a professor of pathology, and John Fox, who was another University of Chicago graduate, had a Ph.D. in pathology as well as an M.D. Fox and I were both at the Rockefeller Institute, and were attending the congress. So we ran into the two professors. "Ah, let's go to lunch, fellows." So the four of us went to lunch. After the lunch, one or the other of them, Hudson or Cannon--I don't recall whom--got the tab. So he passed it over to John and me and said, "Well, you fellows can pay. You're part of the fraternity now." [laughter] In other words, we had made it. We were colleagues. That was just like one of the maturity rites in primitive societies.

So Hudson and I became very good friends, although he gave me a hard time all those years. We had to write quarterly reports, and I could never write one to satisfy him. The English was terrible. Not the science, just the English. He'd blue pencil the report and have me look up words and synonyms in the dictionary and get another word for this or that. He really made me use a dictionary. You see, I've got one over there, and I've got two at home. I always use them when writing scientific papers, often even letters.

Hughes: In your graduate work, you were doubtless pretty heavily into bacteriology, but...

#### Polio Research

Lennette: We worked on polio actually.

Hughes: But the course material was mainly...?

Lennette: It was bacteriology. Yes, as a matter of fact, if you were a graduate student and you said you were going to go into virology, you were considered beyond the pale. You were just nuts. Nobody in his right mind would do that for his thesis. In virology you have to work with animals and it takes forever to do an experiment. The status areas were physiology of bacteria or the genetics of bacteria. But you'd never go into virology. That was a dead-end. So there we were. That's why I'm a pioneer. Nobody was interested in going into something as sterile as that field was.

Hughes: And Hudson started with the polio research simply because the money was there and that's what the lab had been doing?

Lennette: The money was there, yes.

Hughes: What was the Milbank Fund?

Lennette: [Jeremiah] Milbank was a New York banker, and the family had set up a foundation, but it was called a fund, the Milbank Fund. The Milbank Fund actually supported, I think, more projects in economics and in the classics than in science. They supported the polio research. As I say, there was a big sum, maybe four or five hundred dollars.

Our research required monkeys, which at that time were very inexpensive. You could buy a small monkey for about two and a half, three dollars. Now they're about six, seven hundred dollars apiece. That's how I got my start, working on polio. And then when Mr. Roosevelt came into office, his friend and law partner, Basil O'Connor, decided they would have these Birthday Balls. So they were going to have the first one--I don't know when it was.

Hughes: About '34, I think.\*

Lennette: We were running out of money, and we got a telegram one day from Wake Robin, Michigan, from Paul de Kruif. Does that name ring a bell?

Hughes: Yes.

Lennette: He was a very popular writer. He was also a Ph.D. in bacteriology; knew the field. I don't recall how he got involved in the polio business. But anyway, he was one of the top echelon people in this, and one day we got a telegram, I guess it was, saying that they would send us support for our polio work as soon as the Ball money was in and had been counted and everything. "In the meantime I am sending you a check for five hundred dollars to tide you over." Well, that did more than tide us over; it kept up going for quite a while. Then after that, all the money came from the National Foundation for Infantile Paralysis, the March of Dimes.

Hughes: Which was founded in 1938.

Lennette: Yes, somewhere around there.

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\*The first Birthday Ball was held January 30, 1934.

Hughes: Did the funding increase when the March of Dimes came into being?

Lennette: Yes, there were more people who went into the field because Roosevelt was dramatizing his incapacities--not intentionally--but he was dramatizing in the sense that, whenever he got up to get to the podium to speak, it was quite an effort on his part. He was really handicapped. And this gave people some awareness of what the disease was all about.

Actually, economically the disease wasn't very important. Secondly, not many cases were seen in this country. There weren't too many people paralyzed from polio in any one neighborhood, so it never made much of an impact. As a matter of fact, diseases or lesions you couldn't see in the kidney or heart were far more important than these flail limbs of the polio patient. But he made the impact, so there was plenty of money available. And then when they had the support, they worked on other viruses besides polio.

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Hughes: What was the subject of your Ph.D. thesis ?

Lennette: Something on cellular immunity. And I had one hell of a time with that thesis, because I was about thirty years ahead of everybody else. Cellular immunity today is a big thing. At that time, it was all humoral immunity. What's this guy Lennette talking about? I had a hard time defending it.

Hughes: What was your argument in a nutshell?

Lennette: Gee, we're talking about almost thirty-five, forty years ago.

Hughes: Let me back up a little bit. How did you even pick the topic?

Lennette: I didn't so much pick it as Hudson picked it and gave it to me.

Hughes: He was your supervisor then?

Lennette: Yes. He thought it ought to be interesting to work on. Mind you, I had to do all the lab work, all the scut work. He was the brain, sitting in the office, reading all the literature and evaluating it.

Hughes: Was this tying in with the polio work, with a vaccine way in the distance?

Lennette: Yes. People were interested in vaccines in those days. Several people worked on the vaccine at that time, by '37 or '38. There was a young man in New York by the name of [Maurice] Brodie who produced a vaccine which was inactivated by formaldehyde; however,

Lennette: it wasn't quite inactivated, and he had several accidents with it. And then [John] Kolmer, a very respected scientist who developed the Kolmer test for syphilis, also worked on the inactivation of polio virus, and that was with sodium ricinolate. He ran into the same sort of a problem, He had some vaccines in which treatment failed to completely inactivate the virus, and that produced cases of paralytic poliomyelitis.

So for a long time everything was in the doldrums. People were just not geared to producing a vaccine or didn't want to try it, because the source of the virus was the spinal cord of the monkey. That's where the virus was located, just as it is in man. We had to open these monkeys up and take out all of the spinal cord. We kept the virus going by passage from animal to animal. And if you grind up such material, you've got a really crude mixture of all sorts of proteins and polysaccharides and fats of all kinds, just a mishmash of things. So you don't know what you're dealing with, and if you add formaldehyde to something which has been ostensibly pretty well purified by centrifugation, you still have something which is turbid, and you don't know much about the particulates, at least we didn't in those days. You just put in some formaldehyde or whatever and inactivate the virus, and you do a few tests, and if nothing happens in the animal, then you think, well, we've got a vaccine. But you put it into man, who is the ultimate susceptible animal, and then something else goes wrong, and you've got a problem. So Jonas Salk was the right researcher at the right time, because John Enders had cleared the path for him with his tissue culture methods.

Hughes: Were you suspecting in the late thirties, when you were doing this work, that there might be several types of polio virus?

Lennette: We had some suggestion that there would be different types. Francis Gordon was working in the lab after he came back from Martinez. We had done some work, and had a lot of convalescent animals around in the laboratory, animals with paralyzed limbs; they obviously had clinical polio, no question about that. So we would inoculate fresh human material into these monkeys, and occasionally one would come down with a second attack, so that there was evidence of a difference. But our techniques were not good enough to detect them, to work out how different or how closely related they were. But this was done by several people later on.

Sir MacFarlane Burnet, who subsequently was awarded the Nobel Prize and was also knighted, was one of the first people on the scene of strain differences. He had the famous Victoria strain, which he showed was different from the other strains. We didn't know there were three types at that time. That was the first thing to be sorted out before you could make a vaccine. And it was sorted out on the basis of this kind of work. Not that Francis Gordon and I

- Lennette: pursued it any, because we didn't. But people like Burnet did, as did Charles Pait and his mentor, John Kessel, at USC [University of Southern California], and the people at Johns Hopkins, such as David Bodian. They all contributed to this, and they eventually showed there were three types.
- Hughes: Of course, later, I think in the late forties, the National Foundation for Infantile Paralysis put quite a bit of money into the actual typing program. I believe Salk was involved; there were three or four labs involved. I can't remember all the people. There were quite a few people who were just typing.
- Lennette: Sure, that was an important problem.
- Hughes: So I guess it wasn't till the very early fifties that the three types were identified.
- Lennette: It was right after the war that they really began to go straight ahead on this and get some idea of the differences.
- Hughes: Let's talk in more detail about the research that you did at the University of Chicago. In going over your papers of that period-- and I must admit I didn't read every single one--there seem to be three areas that you were working on, usually with Hudson, although I think there were a few papers that you published under your own name. I'm talking about the period, roughly 1932 to 1938, before you start publishing on encephalitis.
- Lennette: While I was still at the University of Chicago.
- Hughes: Right. One of the three general areas that I picked out was the neutralizing effect of various sera that seemed to be collected from all over the world.\*

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\*N. Paul Hudson and Edwin H. Lennette, "The examination of pooled human serum for its neutralizing effects on the poliomyelitis virus." J. Prevent. Med. 6 (1932): 335-339.

\_\_\_\_\_, "Neutralization of poliomyelitis virus by the serum of Liberian Negroes," Proc. Soc. Exp. Biol. Med. 29 (1932): 1090-1091.

Edwin H. Lennette and N. Paul Hudson, "Neutralization of poliomyelitis virus by the serum of native Chinese of Peiping." Proc. Soc. Exp. Biol. Med. 30 (1933): 449-451.

Lennette: That's right. We were trying to find out where poliomyelitis occurred. Now, the background reason for that is everybody claimed--and I mean virtually everybody--that there was no paralytic polio in China. So we got these serums that you mentioned from Peking, tested them for polio-neutralizing antibody, and found perhaps eighty percent of them were positive for antibody. So here was evidence that polio did occur. Subsequently, when people went back into the Chinese villages, and so on, and really looked for paralytic polio, they found it, so what we had was indirect serological evidence that poliomyelitis did occur in those countries presumed free of the disease.

It's always easy to look back and make the conclusions because you have the benefit of today's information. We know today how polio virus behaves, and it's no different in Egypt or in Houston in the low socioeconomic levels than it is in China. These very low socioeconomic areas where the habits are such that there is a continual exposure to contaminated environment, fecal environment, you're going to have a high incidence of infection early in life. But most of that infection is going to be subclinical. These people develop antibody. Joe Melnick and his associates at Houston have shown for Houston and also for Egypt, for that matter, that children are born with antibody from the mother, and by six months they lose all their antibody, then the antibody titer begins to go up very steeply. So by about five years, eighty percent of the children have antibody, then it tails off with age. Now, you take a high socioeconomic level, you've got quite a different pattern. Many of these people never do acquire immunity. And these are the people who get the disease. You see it in adolescents; you'll see it in adults. This was the first entree into that.

Hughes: When you say that you got sera from Peking, exactly how was that arranged? Was this Rockefeller people that you contacted?

Lennette: Yes, some of them. Paul Hudson had contacts with the China Medical Board to send serums over, and we also had some visiting Chinese scientists occasionally who would send us serum specimens. These would come perhaps from studies that they themselves were doing.

Hughes: I believe that there were quite a few from Africa as well, Liberian Negroes, for example.

Lennette: That's right. These came through the Rockefeller Foundation.

Hughes: What was the significance of determining that yes, it was a widespread disease?

Lennette: The prevailing opinion was that this was not a disease of the tropics; it was a disease of the temperate zone. You didn't see it in the tropics. And you didn't, really, because these people were so exposed to a heavily contaminated fecal environment, and thus were immunized early. It's just like chickenpox. Chickenpox in a young child is mild. But in an adult it's a disease not to have, and the same way with hepatitis. Most kids who get hepatitis don't even know it. But the adults certainly get a real severe disease. This is what you had going on a large scale all through Latin America, Africa, and the Orient, heavily exposed to a fecal environment. So the population got immunization early. We and the Swedes, for example, like all Western Europeans, are paying heavily for having cleaned up our environments.

Hughes: What about the breakdown of labor? Were you still pretty much doing all the lab work and Hudson was directing?

Lennette: Oh, he would get in occasionally and help; he didn't have the time, but he did as much as time permitted. If he ever reads this, he'll get a charge out of it. I had to catch these monkeys every day, sometimes twice a day, to take their temperatures after they were inoculated. Sometimes I had fifty or sixty of them to catch, put on leather gloves up to the elbow, opened these cage doors, and got them out of that cage. In the meantime, they were just biting you as fiercely as they could; they'd try to bite through the leather.

He was out there one day giving me advice and suggestions about how to catch these monkeys. It was a hot day, I guess, and I was in no humor to take all this, so I said, "Well, how many monkeys have you caught, Dr. Hudson?" He looked at me and said, "One." [laughter] Later on he told me that in Africa he didn't do such menial work; a white man never did this sort of thing, but left it to the natives. The only monkey he ever caught was on his way back from Africa. He stopped at the Pasteur Institute in Paris, and here was this great, famous yellow fever investigator, and gee, he ought to know all about monkeys, so they asked him to show them how to catch a monkey. He'd never caught one before! [laughter]

Hudson was very deeply interested, and he followed the literature and was very helpful. He'd come out occasionally when he had time to help me with an autopsy. You see, I had to do everything from A to Z. Monkeys would come in from the importer--they would come in from India, a whole crate or two crates would come in--and it was up to me to get them all uncrated and put into individual cages, get a collar on them, and put a tag on the collar so they had a number that we could enter into the book when they arrived, their condition, the temperature and so on, and follow them for a week or two to weed out the ones that were obviously unfit.

Lennette: When we were going to use them, I had to bring them in, shave their heads--really shave them--and then I had to prepare the virus, grind up the spinal cords--we kept the cords in glycerin in the refrigerator--make the suspension, centrifuge it, clarify it and get it into syringes, and drill the hole in the skull, and inoculate the animal. After that I had to close up the lesion with collodion to be sure that they didn't get infected, and put them back in the cage. And from that point on, you took their temperature, sometimes twice a day, depending upon the situation, how many animals you had. Sometimes I couldn't get around to all of them. And as they became paralytic, or as they were developing minor symptoms of infection, you had to record all this in a little bound book. So that was my job, to record all this: beginning paralysis of the left arm, or whatever.

And then when the animal was in extremis, really moribund, we'd bring it to the laboratory and sacrifice it, and then open up the spinal canal--that means you had to use big, heavy forceps, as they do for bone surgery, to open that whole spinal column, peel it back, take out the spinal cord, cut it up, put the pieces into a little fifty per cent glycerin. That went in the refrigerator; it had to be labeled and recorded in the books and so on. Then you snipped off little pieces for cytological examination to see what the lesions were--at the cervical and at the lumbar area. Those were the two major points. Sometimes up in the medulla. You've got these pieces in a little bottle of fixative; then you've got to run them through a whole series of alcohols, dehydrate them, and through a whole series of paraffins or collodion, as the case may be, to the point where the tissue is embedded. It took ten days or two weeks to do this; day by day, you changed the reagents. And finally you had something you could cut on the microtome. You'd mount it on the slide, and you could see it under the microscope. I had to do all this! It is sort of like trying to run a drugstore all by yourself. No help. It was good experience.

Hughes: Meanwhile you were taking courses as well.

Lennette: Yes. But Hudson was not disinterested; it was just that he didn't have the time. He had a teaching schedule, and at that time he had about six or eight graduate students. That's very demanding.

Hughes: What else was he working on other than polio?

Lennette: Oh, at that time they were working on the virus called submaxillary gland virus of guinea pigs, and this was in the thirties. That's a very important virus today, cytomegalovirus--congenital infection in babies leads to retardation. We don't know how big the pool is of retarded children. It's a problem in homosexuals in San Francisco, well advertised. In those days nobody paid much attention to cytomegalovirus. It hadn't reached its day of fashion yet.

Hughes: Why did he single it out, do you know?

Lennette: Oh, it was just a good agent to work with. One of his graduate students, Floyd Markham, who subsequently went to Lederle, thought it would be an interesting virus.

Hughes: Was the Milbank supporting all of this?

Lennette: They were supporting all of it. You know this publication, Current Contents?

Hughes: Yes.

Lennette: We had a Current Contents in our lab. We had a chap who used to go to the biology library every Friday afternoon and photograph all the journals' contents pages, and bring them back on Monday, and we had a Current Contents. This is 1935, '36.

Hughes: Isn't that something!

Lennette: But he couldn't make it pay.

Hughes: The second area of research that I singled out for the Chicago period was work on the portal of entry of polio virus. Of course, it's interesting to read the papers and to realize that you strongly suspected that it was the upper respiratory tract that was the main portal of entry. There was one paper where you mentioned that there could be infection through the gastrointestinal tract, but you felt that that was not the major route. Why did the idea of the upper respiratory tract hold on for so long, for thirty years really? [Simon] Flexner came out with his paper in 1910, and it wasn't really until [Albert] Sabin's work in 1940 that the intestinal route was really accepted as the prominent portal of entry in humans.

Lennette: Well, you have people who become giants in their field, and then pretty soon they become authorities and authoritarians, and whatever they say, it must be so. Just like our popular singers in Hollywood, when they open their mouths to make some pronouncement on the political situation in whatever part of the world, the great bulk of the population accepts this as a fact.

Well, Flexner was a tremendous scientist and director of the Rockefeller Institute for Medical Research. There is no question about his stature as a scientist. But he had his hang-ups. We all do. You have to recognize that. For example, Max Theiler subsequently got the Nobel Prize, as you know, for developing yellow fever vaccine. When Max uncovered a virus in

Lennette: mice which produced in the spinal cord lesions similar to those seen in man or monkeys with poliomyelitis, he called it mouse polio. And Flexner, who was the director of the Rockefeller Institute, said, "No, you can't call it that. Poliomyelitis occurs only in primates, man and monkeys." So what could Max do? He was kind of low on the totem pole. So it came out mouse encephelomyelitis. That's where that term comes from. That's one instance.

Now, let me back off just a moment to show how you can be misled. If you go back to the 1890s--'95, '96, '98--and look at the Swedish literature where most of the studies on the epidemiology of poliomyelitis came from, you'll see any number of papers--most of them by [Ivar] Wickman--on the epidemiology of poliomyelitis, which led to the suspicion that polio might be a waterborne disease. Why? Because all the cases occurred in these little villages along a main stream, a water artery. Well, subsequently we showed that's where the bulk of the population was. They didn't live inland; they lived right on the streams, obviously, because that was a means of transportation winter and summer, and also that was where they got their water.

So that belief went by the boards, and it was thought then it must be respiratory, because of the season of the year in which it occurs. It's kind of strange to have it occurring during the summer if it's a respiratory disease. But that became, for whatever reasons, inculcated in the minds of most of us--myself included--that polio is probably a respiratory disease, passed just like many things, like rubella, measles, or pneumonia, from person to person. This is where all this business came in, like cutting the olfactory tracts. When we did that, there was no disease after intranasal inoculation of virus, and the animal survived.

An extension of that was done by [Edwin] Schultz at Stanford, who used zinc sulfate. He instilled zinc sulfate into the monkey's nose. Something happened to the olfactory apparatus, and the monkeys didn't come down with polio when inoculated intranasally. Of course, when it was tried in man it was pretty horrendous, because it just ruined your sense of smell. So you couldn't use it in man. It was thought that it might be a good prophylactic. You see, this was before the days of the vaccine. Well, that also went by the board.

Now, we had in Cleveland a very fine pediatrician by the name of John Toomey, who was also a pretty good anatomist. He had good training in anatomy, including neuroanatomy. He showed that you could infect monkeys by feeding them polio virus. He wrote some papers which were kind of wild, too. For example, he could show the relationship on a graph between the incidence of poliomyelitis and the harvesting of apples.

Lennette: He really destroyed his own arguments by these sorts of things, but he was trying to prove his point, so you can't fault him for that. At the time we did, but in retrospect, he was trying to prove his point, and it was perfectly all right. And John showed that you can produce polio in monkeys by feeding them virus.

Hughes: When was this now?

Lennette: Oh, this is back in the late thirties, maybe early forties, right after the war, because there wasn't much done during the war period. But he used a different species of monkeys. He used Macacus Cynomolgus, not Macacus Rhesus, which comes from India. Cynomolgus comes from Africa and the Philippines, and it makes all the difference in the world in susceptibility. You can't do anything to a rhesus monkey by feeding virus, as I myself in some of these papers pointed out. We'd just take a loop of bowel and exteriorize it so that you could put the spinal cord right in this piece of bowel and clamp it off so it couldn't fall out, and nothing happened. It got digested; nothing would happen. The rhesus monkey is just resistant to intestinal infection.

Hughes: Oh, is that it?

Lennette: That's the whole point. We just kept missing it. Today it's quite obvious.

Hughes: It seemed a pretty logical conclusion to me from the experiments you'd done.

Lennette: Sure. And then finally Albert Sabin got into the act, and he repeated some of these experiments and found out that you can infect animals by the oral route. Not only that, but you find the virus in the stools of these monkeys if you infect them that way. You also find the virus in the stools of man. It doesn't necessarily come out in the nasal washings; it can come out in the stool.

Hughes: So nobody had looked at the stools before?

Lennette: No. Sabin had the prestige and the stature to open up this whole area, which is what happened. And of course, with a new animal, like the cynomolgus monkey, you could really go to town.

And the third area of research?

Hughes: The mechanism of immunity in polio.

Lennette: Not very much was known about immunity in those days, especially in something like polio, which would be hard to work on. So everybody assumed, because we had antibodies in these various bloods from Africans and Chinese, that humoral immunity must play a very important part, and there's no cellular element--that sort of went out of fashion.

The first person, a pioneer, to emphasize cellular immunity was Elie Metchnikoff in Russia, way back in the 1880s or something like that. He was just fifty years, seventy years, ahead of his time. The sorts of things he was doing just fell into limbo, and everybody forgot about them. Humoral immunity was the big thing, so everybody focused on humoral immunity, including our laboratory. But we thought there might be more to it, so let's take a look at it. Hudson thought that this would be a good project for me, and that's where I got involved in it.

We would do things like inoculate a monkey, let's say intravenously, with polio virus, let the virus circulate, and then go in and take out the spleen or tie it off, and then perfuse it and see if antibody had formed in the organ or see what the cells looked like. Well, that was pretty amateurish stuff, because we just didn't have the techniques to plow unknown ground in the 1930s. But we were headed in the right direction. And that's why I had such a hard time defending my thesis. If it hadn't been for Hudson in the other corner--it was also his work, too, so he had to defend it--I probably wouldn't have gotten by the examining committee for my doctoral degree.

Hughes: Who else was on the committee?

Lennette: Oh, there was a parasitologist, a pathologist, and somebody from physiology, as I recall.

Hughes: And they were set against it from the beginning just because it was a cellular approach rather than a humoral?

Lennette: Well, they didn't think that I was proving my point. They were willing to accept that it might work, but I hadn't shown it. I guess in large part I hadn't.

Hughes: But you did pull through.

Lennette: Oh, I pulled through, yes.

Hughes: Is there any more to be said about the polio research of that period? Or Chicago in general?

Lennette: Yes. I was taking both degrees at the same time, and I received my Ph.D. in '35 and the M.D. in '36. Now I was ready for an internship. I needed some money, too. Poor as a churchmouse. I got my M.D. in December. We had commencement four times a year at that time. So I stayed on the staff of the department of bacteriology for the next six months--till July of 1937--as an instructor in bacteriology.

About the same time, Paul Hudson was discontented with his situation in Chicago. He was on the faculty, and there was a new chairman about to be appointed, bypassing him, so he accepted the deanship of the graduate school at Ohio State. And he was, of course, faced with building up a department. It wasn't much of a department in size there in microbiology, so he was taking some of his Ph.D. people with him. I was a little unhappy because I wasn't one of the group that was going to go to Ohio State.

Hughes: Why was that decision made--because you needed to stay and finish up your M.D.?

Lennette: Yes. I had my Ph.D., and was anxious to go to Columbus, Ohio, and so I challenged him on that. "How come you're taking all these people and you're leaving my behind? What's the problem? What do you have against me?"

He said, "Nothing, except I think you should stay here and finish your M.D." I had another year to go. "Finish your M.D., and then get your internship, and then get your license." Well, I needed money. We were all poor as churchmice. We had gone through college, through graduate school, through medical school--we never had two dimes to rub together, and we were getting tired of being paupers all the time. Mind you, I'm getting close to thirty at this time, and hadn't earned a nickel. That was the best advice I ever got, in retrospect. He just wouldn't take me.

He said, "You're working on an M.D.; you stay here and you get that degree." And I've thanked him for it ever since. He still chuckles when I tell him about that. So he went to Ohio State and took several people with him. One was a young fellow who had been working on plant viruses, who subsequently became chairman of the department of microbiology, succeeding Hudson who went to Ohio State as chairman of the department and subsequently became dean of the graduate school. And then I interned at St. Luke's Hospital in Chicago July '37 to July '38.

*Upper Left:* Graduate school in the department of bacteriology and hygiene, 1934 or 1935.

*Lower Left:* Edwin H. Lennette's laboratory in the department of bacteriology and hygiene, ca. 1934.

*Upper Right:* Polio research with laboratory assistant, Robert Johnson, and monkey, 1932 or 1933

*Lower Right:* Graduation from Rush Medical College, 1936.





## II EARLY CAREER

Washington University School of Medicine, St. Louis, 1938-1939

Lennette: I got this telegram from Dr. Rivers. Well, in those days, as I should point out perhaps, things were quite different from today because a professor in this country, just as in Germany, was a highly respected individual, and you didn't argue with him. You did as you were ordered. If you didn't like it, go somewhere else. So these highly-placed scientists, like Tom Rivers, who were internationally renowned had considerable clout and exercised it.

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One day in the spring of 1938 I received a telegram at St. Luke's Hospital to "proceed to Washington University, St. Louis. Two positions available. Take your choice." In other words, you're going to be employed, go on down and get a job. I couldn't even raise the three and a half dollar train fare to go to St. Louis. It was a real sacrifice. My wife was working, and so we finally scraped up the train fare. What is it to St. Louis, about three hundred miles, something like that, from Chicago?

So I went to St. Louis and was interviewed in the department of pathology the first day and the department of microbiology the second day. Two very eminent people were the chairmen of the departments. One was Howard McCordock in pathology, and the other was Jacques Bronfenbrenner, whose name is well recognized outside microbiology because his son is now a well-known sociologist. Jacques was a pipe-smoking, typical scientist, and a very nice person. So both of them offered me a job. Here I am with the dilemma, which one should I take? Actually by training I'm not a pathologist. I'm really a microbiologist, well, a virologist--I'm nothing. [laughter] So I decided I'd go with Howard McCordock and learn some pathology. It would mean some more training for me. So that's how I got to St. Louis from Chicago.

Hughes: Now how had Rivers singled you out in the beginning?

Lennette: He knew of me because of papers that I had presented at various meetings of the American Society for Microbiology. And, mind you, virologists weren't all that common in those days. So if you heard a virus paper by some young beginner, you knew who he was. There weren't hundreds of virologists. I don't flatter myself that I was eminent or anything. I think it was just such a small group.

Hughes: But Hudson and Rivers didn't have any extraordinary contact?

Lennette: No, except in the usual course of business, various meetings. They were fellow scientists, and of course they knew each other because Paul had been at the Rockefeller Institute for a while. So this is how Rivers knew about me.

Well, he wired me because Howard McCordock had a young fellow by the name of Joseph Smadel, who later turned out to be quite a scientist. He had been working on St. Louis encephalitis. Joe was sent up to New York to learn virology with Rivers. Rivers accepted him, and at the end of the first year, Rivers said that he didn't think that Joe had learned enough; he'd better stay another year. Well, Howard McCordock wasn't too happy about that. But he figured, well, he can go along. So the third year coming up he got another phone call, this time from Rivers saying that Joe was a very fine scientist; he was going to offer him an appointment on his staff. "But don't get all upset," he said, "I'll find you a replacement for Joe." And of course Howard said, "Where are you going to find another guy like Joe? He's very valuable to us. His wife lives here, is on our faculty, and comes from a very prominent St. Louis family." She came from the Moore Paint family--a very nice woman. She was a very good pathologist, too, as well as a teacher. "Well, don't worry; we'll supply you with a body to take his place." So Joe stayed in New York at the Rockefeller Institute, and that's how I got this telegram. Well, I wasn't going to say, "I'm not going to go." This would have been the kiss of death for my career, especially in virology.

Hughes: Get Rivers against you and it would have been.

Lennette: Sure, because he was placing all the chairmen of the departments in microbiology at that time. He had a tremendous amount of influence. So I was told to go to St. Louis and accept the appointment.

[Interview 2: September 23, 1982]##

Lennette: This was at the end of my internship at St. Luke's Hospital in Chicago. So as soon as I finished my internship, which was in July, we--my wife and I--went to St. Louis and found an apartment, which was huge. At least it was to us, because we had no furniture except the few incidentals that one needs for survival or for rather primitive living as a poor student. Of course there was no air conditioning, so we had our problems with that. In any case, we moved to St. Louis; got there about August.

Margaret Smith and Cytomegalovirus

Lennette: I had a laboratory, shared it with Dr. Margaret Smith, who was on the faculty, a full professor. A remarkable woman. I think if she had been born later, she certainly would have been the chairman of the department. She was that kind of person. Never married, but had quite a rapport with the house staff. A good teacher, above all. I learned a lot from her during the brief tenure of that appointment. So Margaret and I got to be fairly good friends.

Unfortunately, my appointment came to an end when Dr. McCordock one day collapsed in the photo darkroom and died of a heart attack. Apparently he had known he had this condition for some time, and from the stories I heard, ostensibly he was treating himself--digitalis. There was no great dissemination of this information, so most people didn't know about it. In any case, during the succeeding weeks and months the university looked for a successor, and finally the dean's office, I guess, came up with several candidates.

The new chairman of the department was to be Robert Moore. He was still a young man professionally and in age. Of course at that age you feel your oats, and he made it pretty clear to everybody concerned, including me, that he was going to run that department. I was young and feisty, too, and nobody was going to tell me how to run my affairs. Nobody was going to take my budget, which wasn't very large. Nobody was going to disburse my funds. I was going to do that myself. It came to the point where somebody had to leave. Obviously, it wasn't going to be the new chairman, so it would be I.

Lennette: But in the meantime I was doing all the virology in the department of pathology. Well, not all of it, because Margaret Smith had grant money to work on cytomegalovirus of mice and guinea pigs. And for some years she was successful in obtaining funds, even after I left. Her work was of some interest to the staff, so she continued to work on that. But interestingly enough, eventually she could not get financial support from the National Institutes of Health, because the study sections in their omniscience couldn't see that her virus had very much bearing on human medicine. Why should they be supporting this research on submaxillary gland virus, dealing with a virus which was primarily in guinea pigs or in mice?

Well, you know what cytomegalovirus infections are today-- one of the areas of great interest financially and scientifically. So Margaret was just ahead of her time.

#### Encephalitis Research

Lennette: I was working on St. Louis encephalitis because most of my background in virology had been in neurotropic diseases. At Chicago, I had been working on poliomyelitis, as I mentioned earlier, so this was just a natural carry-over to St. Louis encephalitis. Our research was concerned with the immunologic aspects, but we had a broad interest in the whole problem.

One morning--it was a Sunday morning--Margaret came to the laboratory very early, around six thirty, seven o'clock as I remember, walked through the autopsy room, and there was a postmortem being carried out on a very young baby, around six weeks old, and Margaret, like a true scientist, inquired what was going on. The resident thought this was a case of encephalitis. So Margaret sampled some brain tissue, brought it up to the laboratory, and gave it to me. She said, "It would be interesting to put this into some mice and see what happens." Well, what happened was that we isolated herpes simplex virus. This was the first proved case--underline proved case--of encephalitis due to the herpes virus. There had been a lot of literature published, but nobody every had any real proof until Margaret came along with these tissues, and we worked all that out.\*

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\*Margaret G. Smith, Edwin H. Lennette, and Harold R. Reames, "Isolation of the virus of herpes simplex and the demonstration of intranuclear inclusions in a case of acute encephalitis." Am. J. Path., 17 (1941):55-68.



*Left:* Edwin H. Lennette on right, intern, St. Luke's Hospital, Chicago, 1937 or 1938



*Left:* Intern, St. Luke's Hospital, Chicago, 1937 or 1938



*Left:* Margaret Smith and Edwin H. Lennette, Washington University School of Medicine, St. Louis, 1939



Lennette: We had an interesting year there. Of course in the interim a number of other developments came along, which made my tenure so unstable.

The International Health Division of the Rockefeller Foundation,  
1939-1946

Lennette: About that time Albert Sabin, whom I knew fairly well--he was at the Rockefeller Institute--suggested to the director of his laboratory... The Rockefeller Institute, as you may know, was divided into small laboratories, just as laboratories are on any campus. Albert was working under Peter Olitsky on neurotropic viruses, actually polio as well as the encephalitis group. Albert suggested to Dr. Olitsky that it might be interesting to have me come up and join that group, that I was available. So then we began to negotiate. I was really not in much of a position to negotiate. I wasn't going to have an appointment come September. But we negotiated on salary and so on. After all, I was not going to leave Washington University with my munificent salary of \$3000 a year for a salary which would be around twenty-one or twenty-two hundred dollars, a pittance, especially in New York City.

In those days you were not expected as an "apprentice" to make a real living or to accumulate funds through your position. You were there to learn, and you had to sacrifice. Far different from today's philosophy of graduate students, or professors, too, I guess. So we couldn't come to an agreement. I think Dr. Olitsky and Dr. Sabin both felt they would like to have me there, but they couldn't convince the administration that I ought to get some additional funds.

Hughes: Are you saying that the Rockefeller Institute underpaid most other institutions?

Lennette: Yes, but these were training positions, akin to internships. I guess it's analogous to some of the fellowships today. But in those days you came in for a pittance. The chairman of the department in those days made perhaps ten thousand dollars a year as a salary, which isn't much by today's standards, but at that time it was considerable. You could buy a big home in Long Island for that kind of money. You had to have either an M.D., Ph.D., or D.V.M. Usually we were M.D.s in those days. You came in, and you got eighteen hundred, two thousand, twenty-one hundred dollars a year, which was just enough to keep body and soul together, and if you had a family to support, you had a hard

Lennette: time making it from one pay period to another, believe me. If you give these young people a hard time financially and otherwise, this builds character. That was the philosophy.

Well, I just couldn't see coming down in scale. After all, it's easier to ask for additional money--if you're earning three thousand dollars, ask for four--than it is to ask for four when you're making eighteen hundred. The gap is too large.

Hughes: So even the prestige of the Rockefeller Institute wasn't enough to make you rush there for a lower salary?

Lennette: No. Although they did have the prestige. That was the place to be, because it was the premier research institution, recognized throughout the world.

Hughes: In any of the sciences, or particularly in virology?

Lennette: The biomedical sciences, because they had an excellent group of people doing biochemistry, physiology, biology, microbiology--outstanding, internationally-renowned people.

Hughes: And a reputation already in viral research, too.

Lennette: Yes, that's where a lot of it was begun. Tom Rivers was a Georgia boy, a pediatrician, who was interested originally in chicken pox. He came to the institute as a young man, and began to work in the virus field, about which virtually nothing was known, so he was a true pioneer. A lot of his early work was laying the foundation for medical virology. So that was the place to be in those days.

Funding by the Rockefeller family was such that you didn't have to worry about outside funds of any kind, so I would have been delighted to be there. I would be pleased to be there on the staff, but I had obligations to my family. I didn't know where I would go. In any case, we couldn't get together. This was all on a friendly basis. There was no animosity involved.

So one day I got a letter from Albert Sabin saying that he and Peter Olitsky were sorry we couldn't get together because they would have liked to have me in their group. Herald Cox was a part of the group there at the time, and maybe Jerome Syverton, who subsequently became chairman of microbiology at the University of Minnesota. So they were turning me over for consideration by the International Health Division of the Rockefeller Foundation.

Lennette: The Rockefeller Foundation had one floor at the institute in the North Building. Its staff was working primarily on yellow fever, making a vaccine, and also doing research on yellow fever. In addition, they were doing some research on malaria and on influenza. They were just beginning the influenza work with Frank Horsfall in charge. So it would be interesting to work in a laboratory with such a program; and also with the prospect of doing some work in the field. That sort of appealed to me.

So I came to New York, was interviewed by Dr. Wilbur A. Sawyer. Sawyer then sent me uptown to the Rockefeller Institute to talk to Johannes Bauer. Bauer was a Swede who worked for the Red Cross during the First World War and was concerned with the refugee problem, and was then taken on the staff by the International Health Division. The International Health Division of the Rockefeller Foundation was the formal name. So Johannes ended up in New York as the chief of the laboratory. He also was a tall, very aggressive, very opinionated individual. I'm not being derogatory. He was a good administrator. But he was very impatient. So he ran that lab with an iron hand.

Hughes: The whole International Health Division?

Lennette: No, just the laboratory. Wilbur Sawyer was the director of the International Health Division, and Johannes Bauer ran the laboratory housed in the Rockefeller Institute. The offices of the Rockefeller Foundation were in the RCA building on West 50th Street, fifty-fourth floor, and from there they had their public health and research empire all over the world, where they had considerable weight in various countries. It was interesting. It served a very useful purpose, I think. The foundation never got full credit, in my estimate, for all the things it did for mankind. It didn't want it. It always kept a low visibility. But they did some wonderful things, especially in malaria and hookworm in the south--that's how they started, working on hookworm--and then they went into malaria, which was and still is a great problem.

Well, Johannes gave me a hard time. He introduced me to the staff and got a lot of information out of me, what I was doing, what I wanted to do, and so on. They decided maybe I could cut the mustard, so I was offered an appointment, which I accepted. And then later on, as I think I mentioned earlier, I was a little annoyed because I wasn't offered the same salary as Monroe Eaton, who was also a predecessor at Washington University. Eaton was a Yale Medical School graduate, a native of Stockton. He was on the staff of the department of microbiology with Bronfenbrenner, so you see when he left there was

Lennette: another hiatus there. In any case, Eaton received a salary of a thousand dollars a year more than I. After all, he had had more experience, and so on, so I guess that made the difference, but that irked me.

#### Rockefeller Personalities and Research

Lennette: Now Wilbur Sawyer I'll mention momentarily. He was quite an interesting person. He had been the director of the Division of Laboratories for the Department of Health in California back in World War I. Subsequently he worked in the laboratories of the Rockefeller Foundation abroad, and then he eventually achieved the directorship of the International Health Division. Very kindly, very courteous person.

When we arrived in New York and I took up the position, the Sawyers already had a house for us up at Hastings On Hudson, which, if we were interested, we could rent, which we did. And then when we actually arrived on the scene, they got us to the house, where they had brought groceries so we wouldn't have to scurry around. I thought that was very thoughtful, especially for somebody in his position, to take the time to do this for some lowly staff member who had no clout of any kind. The whole Sawyer family was that way. So I enjoyed working with him.

They were also our neighbors; we had a little enclave up there. Wilbur Sawyer lived down the road a couple of blocks, and down a little further was Max Theiler. He subsequently got the Nobel Prize for his yellow fever vaccine work. Lowell Coggeshall headed the work on malaria and eventually returned to the University of Chicago as dean of the division of biological sciences and eventually became a vice president of the university and a member of the board of trustees. As far as I know, he is retired and still living in Alabama somewhere. And then there was a pathologist living in Hastings, Bob Huntington, who was on the Cornell faculty, who came out to California as pathologist for Kern County General Hospital. So there was a little enclave of us. Rene Dubos, who lived in Dobbs Ferry, was one of our commute group, subsequently achieved international renown as an ecologist and elder science statesman.

We lived in Hastings. That was a commutation job, and I was unaccustomed to having my time decided by the clock. The railroad decided what time you were going to go to work and what time you were going to leave. If you wanted to get to Hastings On Hudson, you'd better get the right train or you'd be in

Lennette: New York all night. So my hours were constricted by that, plus the fact it took an hour and a half each direction to get from Hastings to the institute. I didn't mind that too much originally. Later it got to be rather a chore.

#### Influenza Studies

Lennette: I was assigned to work with Dr. Frank Horsfall, who had just come to the foundation from the Rockefeller Institute.

Hughes: Now did Sawyer make that decision?

Lennette: He and Bauer needed somebody, because Eaton, who had been working on influenza, was moved out here to the West Coast--actually to Berkeley. Now the reason I mentioned a little earlier I'd like to tell you about Sawyer was his contribution to this laboratory. Influenza was a brand-new virus. This was 1939 we're talking about. I had just arrived in New York, just a few days before World War II broke out. Poland was invaded. And the Britishers who were visiting scientists all had to pack up and return. I remember it very vividly.

Influenza virus had been discovered in 1933. With virus work being so dreadfully expensive and so time consuming, so slow to give results, the foundation felt this was its sphere, because it could contribute the money; it could get the staff together, and it could study influenza--especially influenza--and other respiratory diseases in depth around the world. Through the International Health Division--I imagine it was probably again Sawyer's interest; I'm not sure--they set up a laboratory in Budapest, Hungary, under Dr. Richard Moreland Taylor. Taylor was interested in epidemiology and also in the laboratory, so he established a laboratory in the school of hygiene in Budapest.

Hughes: Why Budapest?

Lennette: It was sort of a central spot, I imagine. I don't know all the reasons why it was chosen. I think today if they were going to do this, it would probably be Geneva, because Geneva is central to European points. Perhaps the interest of the Hungarian government might have been a determinant.

And then a laboratory was also opened in Minneapolis with [E.R.] Rickard assigned to work there as project director. I think the laboratory was started by Clara Nigg. I'm not sure of this. Have you talked to Clara?

Hughes: I have.\*

Lennette: I think she started the laboratory, but I'm not positive.

Hughes: Yes, she did.

Lennette: The reason I say that is I worked with Rickard in New York, and eventually he was assigned to Minnesota. I don't know whether he'd been there twice or just the one time.

Hughes: I don't know that part.

Lennette: He was an epidemiologist, not a laboratory person. I enjoyed working with him in the field out of New York, because I worked with Horsfall in the laboratory, and Horsfall wasn't teaching me any new techniques. He had brought me in as a junior colleague because I was using methods that weren't all that difficult or all that sophisticated. They were pretty mundane and simple because we didn't have very much knowledge in virology.

#### Early Virological Tests

Hughes: Could you run through what they were?

Lennette: Well, we really had only two good tests. A third one came along later. We had a neutralization test, which measured antibody. It could be used to measure antibody response or, conversely, if you had known antibody, you could identify a virus. So the neutralization test was the basic and fundamental tool, and still is, in large part, today. This was the test on which you based your comparisons of other methods, to see if they would agree. If they didn't agree with the neutralization test, the chance was there was something wrong.

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\*The transcript of the interview with Clara Nigg, recorded September 9, 1982, is on deposit at The Bancroft Library.

Lennette: The neutralization test actually was first used about 1898 by [George M.] Sternberg. Sternberg was a pathologist working in the army medical corps, and based at Walter Reed Hospital. He showed that if you mixed vaccinia virus along with immune serum, say serum from a patient with smallpox, the infectivity would be neutralized for an animal. That was called the neutralization test because infectivity of the virus was neutralized.

The other test, the complement fixation test, was based on the work of [Jules] Bordet, a Frenchman. It goes back to the early days of the century also--1910 or something like that. Maybe earlier than that. That test depends on bringing together antibody and the viral antigen in vitro. If there's a union of specific antibody with this particular virus, there's no way to show that the union has occurred unless you add complement from a guinea pig. Then you add red cells that are sensitized by what we call hemolysin. Hemolysin is antibody to the red cell. The point is that complement is the middle piece that is required either for fixation or for nonfixation. If it joins with the specific serum and the specific antigen, then you get a positive test. Nothing happens to the red cell. On the other hand, if this is not specific, then the complement freely unites with the hemolysin to destroy the red cell, so you get a clear pink solution.

Everybody was scared of this test and still is today, scared to death of this, because it is such a complicated procedure. I could never see that. I thought it was a very simple test. For some strange reason, everybody abhors this test because it seems so difficult.

So these were the two techniques available until George Hirst came around and invented another method. He's the father of the hemagglutination test. That in itself is interesting, because George came from Homer Swift's laboratory in the Rockefeller Institute. He had been working on streptococcal diseases. George came over to our building, and Frank didn't know what to start him off on at the moment, because we were pretty busy. We were trying to develop a vaccine against influenza, doing it the wrong way around. Anyway, George came to the institute to work with Frank also. So Frank put him to work on a problem, which just continually annoyed us, him and me, because every time we would open these infected eggs, if we weren't careful and cut a blood vessel and the red cells came out, and if influenza virus was present, these cells would all hemagglutinate. It kind of messed everything up. You wanted a nice clear viral solution. So Frank and I thought this would be a good problem for George to work on, which he did. And that came to be the hemagglutination test. He discovered the fundamental principle and a new viral phenomenon.

Lennette: I can always remember that, because I just wasn't astute enough to look into that problem. Frank and I were off on other things, but George came up with this test and really worked it out. He did a good job. He got all the details over the succeeding years. We owe him a great debt for that.

So the complement fixation and neutralization tests were really the only two tools we had. The neutralization test was done in mice by inoculating dilutions of serum against dilutions of virus, as in antibody surveys. Frank worked out sort of a curve, so that if you knew how much virus you used, you knew how much antibody it would take to neutralize it, and that was very basic work. That was just before I came. That has stood up over the years as sort of a model for some of the other viruses which were being titrated.

I was there for two years, September 1939 to June 1941, working on influenza.

Hughes: What about Tommy Francis?

Lennette: Francis left about that time.

Hughes: You're right. He left in 1938 for NYU [New York University].

Lennette: I thought I remembered that correctly, because Monroe Eaton left about the same time. He came out here to Berkeley.

Hughes: Actually, Francis maintained some sort of association with the International Health Division until 1941, but physically he was at NYU.

Lennette: Tommy was at NYU as professor and chairman of microbiology there, and that's where Jonas Salk came in. Jonas was a graduate student under Francis. Francis was one of the moving spirits of influenza; he and [T.P.] Magill had done a lot of teamwork on flu. When Francis was leaving, that's about the time that Frank Horsfall came in from the Rockefeller Institute to take over. Horsfall already had a very good reputation as a scientist.

Hughes: That's the work on type A influenza?

Lennette: He and his associates--this included Ken Goodner. Ken made yellow fever vaccine in the foundation's New York laboratory. Horsfall and Ken and several other people at the institute and the foundation had worked on antisera to pneumococcus. They were finding various other types--there used to be type 1, type 2, type 3, then there was a group 4. Everything that didn't fit into the first three types went into group 4, and eventually

Lennette: they began to sort them out. The importance of sorting it out was that you could make antiserum, say in rabbits, which was done, for the typing of these organisms. Then you would know what the infecting organism was. Later on they began to make immune serums which were used for treatment.

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And then when antibiotics came along, this was the end of the serum business. All that work--and it took several years of real hard labor--was just dissipated, went down the drain.

Hughes: In 1936 the International Health Division took over Francis' work on flu. He'd been working along since the early thirties.

Lennette: Yes, he had done all his research and clinical work in the respiratory disease field. He was a recognized authority on--not only influenza--but also on pneumococcal and streptococcal infections. He was brought into the foundation in 1936 to take over the influenza work. As I said, the flu viruses were uncovered in 1933. Here is an individual with a wide background in respiratory disease, recognized as a scientist, very capable, highly regarded. It was horrendously expensive. Even in those days budgets were something.

Hughes: Was there any particular reason for 1936 as opposed to earlier as far as the International Health Division was concerned?

Lennette: No, I think it took a little while for enough literature to accumulate to show what could be done with a virus, growing and studying it in detail and heading toward a vaccine. That's about the usual time period. If we discover something today, it's written up in the literature, but it's ten years before the clinician takes hold of it in his practice. There's always that long gap in between. So three years isn't too long.

Hughes: I notice that most of your influenza paper were written with Horsfall. Could you say something about the nature of your collaboration?

Lennette: Our collaboration was very good. Frank was sort of a difficult person to work with, because he was always so aloof and distant. I don't know why. He was that way with everybody. It was hard to communicate. There was no question about what a fine mind he had. We could sit down at a table like this; he would go over an experiment. He did a few of them; I did some, and some we did together. We shared the workload between us. At first I found it difficult to approach him because he was always so distant, not in the sense of superiority or anything, that's

Lennette: just the way his genes operated, I guess. He didn't intend to be that way. But we got along very well. (Usually I have no trouble getting along with my colleagues.)

There was some personal dissension on the staff. Monroe Eaton had difficulty with Coggeshall; I don't know who was at fault. And then Monty dropped his malaria research and went over into the influenza and respiratory disease field. He was pretty much alone on that in New York.

When Wilbur Sawyer decided we ought to have a laboratory here in Berkeley just as we had in Minnesota, the natural person to send out here would be Eaton, who came here in 1939. He left just before I got to the institute, and opened up this laboratory. As a matter of fact, we had one person on the staff here who had worked with Tommy Francis on a graduate degree in Michigan, Dorothy Beck. Dorothy was sort of running the laboratory until Eaton came out and then took over. He did some very good work while he was here, before he left to become a professor of microbiology at Harvard. You see, I'm always following somebody somewhere. [laughter] I'm never on my own. I just get into this vortex, and I end up doing something I hadn't anticipated.

So Eaton came to Berkeley in 1939, and set up the laboratory. It wasn't very large. It was on Acton Street, that little green stucco building that you see down at the corner of University Avenue. It was rather interesting because the foundation had bought the land and put up that building--there was a small building in the rear of the lot--for something like ten thousand dollars. This was '37 or '38. Then when I arrived in 1947, when I came back the second time, we had to do a lot of repairs to the building. It cost us seven thousand dollars just to replace the flooring, so you can see how prices had gone up.

We had a garage in this little courtyard. The entrance was from Acton Street. You came in this driveway, and then there was a little garage there where Monroe kept a Plymouth coupe. It had a deadly stench, because he used to transport ferrets in the rumble seat, or whatever you want to call it, and you could hardly bear to get in if the windows were up.

When I came back in 1947--this is jumping in history--the U.S. Public Health Service wanted to put in a laboratory for industrial engineering and toxicology, so they closed off the driveway on Acton Street by putting another laboratory building in there, and made the whole structure L-shaped. We also had a nice victory garden on University. We bought an adjacent piece of land which was made into a driveway, with a garage on it, west of the laboratory. That plot of land alone cost us ten thousand dollars.

- Lennette: This was in 1946, so you can see what that building is worth today. It's owned by the state, a gift from the foundation.
- Hughes: I wanted to talk in a little bit more detail about your research on flu. I was interested particularly in a couple of papers that you wrote on a complex vaccine.\* Was it an accidental discovery, this business of the canine distemper and the flu virus producing it?
- Lennette: No. I don't know how to word this so it won't be misconstrued. We were just getting into mouse work as a study tool. Most of the influenza work for some years, even afterwards, was done on ferrets. Ferrets seemed to be a natural animal for influenza, not in the sense that it occurs amongst ferrets, but in the laboratory it was the animal par excellence. So we used large numbers of ferrets, the virus being found in two places, in the spleen and also in the nose, specifically, in the turbinates. Well, obviously you could get a lot more virus out of the spleen; it was a large organ. So we decided we would use the spleen, and we just inactivated virus in splenic suspensions with formaldehyde. Unknownst to us, there was also present lymphocytic choriomeningitis virus. Well, first of all, you don't make a vaccine from tissues containing an extraneous agent. You can look back at some of the dumb things that were done in 1940, but we didn't have any prescience at that time. We just were learning the hard way. We didn't have any tools. Apparently the vaccine worked, but it wasn't all that good. And when we found it had LCM [lymphocytic choriomeningitis] virus in it, we stopped using it.
- Hughes: But you did try it on human volunteers?
- Lennette: Yes, we tried it around the institute. We did some work in Puerto Rico. I went down to Puerto Rico, where we had a big epidemic of flu, to test the vaccine in a small trial. Incidentally, that vaccine also had bacteria in it, although these too were inactivated. They were a very common, garden-variety bacterium, Bacillus subtilis. But that would not be condoned today. Of course we were working outside of the FDA [Federal Drug Administration], and there were no standards for clinical trials of a viral vaccine. The standards today are quite different. So we could be berated for all these things. It's always much easier to judge with hindsight than the actual performance at the time.

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\*F.L. Horsfall, E.H. Lennette, E.R. Rickard. "A complex vaccine against influenza A virus." J. Exper. Med., 73 (1941):335-55.

Frank L. Horsfall, E.H. Lennette, E.R. Rickard, and G.K. Hirst. "Studies on the efficacy of a complex vaccine against influenza A." Pub. Hlth. Rep., 56 (1941):1863-75.

Hughes: So you stopped the trial voluntarily when you found the second virus?

Lennette: Yes, we hadn't done too much testing. We were just measuring the antibody response. We never had a large enough group that we could follow to see whether they developed influenza subsequently or whether the vaccine actually protected against infection. We just studied the antibody responses, which were not too bad. But everything militated against that. So I was in Puerto Rico--I don't know--about six weeks or so. But out of that came by serendipity another find.

I was doing most of the diagnostic work, the immunology, the antibody work at the institute, so I got to set up all of these tests. We saw in Puerto Rico, for example, what Francis had also seen. You would have an outbreak of influenza, and in some patients you could isolate what we called influenza virus. Other patients yielded nothing, which was rather strange. Or in another episode of what clinically was influenza, you couldn't get a virus. Well, I ran into the same thing in Puerto Rico. Some of the material went to New York and we'd get influenza virus. Out of the others we didn't get anything. About this time Francis had recovered what would later be known as influenza B virus.

Hughes: 1940.

Lennette: Yes. Interestingly enough, he got it from children at a children's home here in San Mateo. These sera had been stored for some years, and he went back and tested them, and they reacted against the influenza-like virus, which he and Magill had described, so we had a second virus now. I published a paper on influenza A and the fact that you had these other diseases which resembled influenza A, but you couldn't get a virus out, and here we had influenza B, so I postulated that there would be other viruses that would produce influenza, so we should call them influenza A, B and C. I didn't put that into the paper. I just mentioned that to Frank, who was way ahead of me. So out of that came a paper between the British and American collaborators. We had people in London on this publication. Most people have forgotten about this publication, which appeared in Lancet.\*

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\*F.L. Horsfall, Jr., E.H. Lennette, E.R. Rickard, C.H. Andrewes, Wilson Smith, and C.H. Stuart-Harris. "The nomenclature of influenza." Lancet 2 (1940): 413-414.

Hughes: That's the one on the nomenclature.

Lennette: Nomenclature. Influenza A, B, and then later on Dick Taylor picked up C, which gave us reason to suspect there might be other types of influenza virus. As we get better and better in our molecular biology and immunology, we can detect differences which were not readily visible early on. In any case, there was A, B and C. Just like we're finding out with hepatitis now, there's hepatitis A, hepatitis B, and the delta agent. Then there's non-A and non-B, whatever in the Lord's name that might mean. It's probably a potpourri of everything under the sun, and will be costly and difficult to sort out. So it was by serendipity that we found this situation with flu virus. That paper proposing a nomenclature was very well accepted.

Hughes: You were also involved in some epidemiological work, and that's where Rickard came in. Were you doing the diagnoses?

Lennette: Yes, I was doing all the antibody surveys and virus isolations in the laboratory. Rick was out in the field seeing people who were ill, and getting specimens on them, trying to trace the chain of infection and so on. He was very good at that. So I went with him several times, because I had a lot of respect for his ability. I wanted to learn something about epidemiology, and so I learned the fundamentals from Rick, not in the classroom, right on my own two feet. He was very good.

Hughes: One of the things that came out of those papers\*--I think there were two or three on the Yorktown study--was that in any given outbreak there usually are both type A and type B viruses involved. Was that something new?

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\*E.R. Rickard, Edwin H. Lennette, and Frank L. Horsfall. "A comprehensive study of influenza in a rural community." Pub. Hlth. Rep. 55 (47) (1940):2146-2147.

E.H. Lennette, E.R. Rickard, G.K. Hirst, and F.L. Horsfall, Jr. "The diverse etiology of epidemic influenza." Pub. Hlth. Rep. 56(36) (1941):1777-1788.

- Lennette: That was a new finding. I mentioned that in the paper that I wrote based on the Puerto Rico study.\* You see, we already knew about B. People used to tell us, and they still do, that you can differentiate clinically between A and B. You can't differentiate. I never was able to, at least. And I don't think Rickard ever could, and he saw a lot of patients.
- Hughes: Did these findings feed directly into your work on production of a vaccine?
- Lennette: Yes, because we all worked together. We used to have periodic meetings. Rick would come in to New York City to meet with us. We were quite a team. Frank was a good team leader, highly respected.
- Hughes: Could you say something, too, about how the team and the International Health Division as a whole related to the rest of the Rockefeller Institute? Was there much coming and going?
- Lennette: No, there wasn't--well, in a sense there was. It depends on how you want to define it. The Rockefeller Institute was a separate entity. It owned all the buildings and the grounds, and was separately endowed; its endowment came from the Rockefeller family, just as the Rockefeller Foundation was also endowed by the Rockefellers, but separately. Each had its own operating funds. The institute was really what you would call the intellectual unit. It was all research, much of it very basic biochemistry, immunology, whatever. Whereas the International Health Division of the Rockefeller Foundation was more field minded, practical minded. They were closer to the information, closer to the clinician. They were closer to the epidemiology, closer to the field. So in this way they complemented each other.

Now the foundation had only one floor, a laboratory floor, in the North Building of the institute, but we used their facilities. There was what you'd call a doctors' dining room, where the staff of the foundation would meet with their peers and colleagues in the institute, and that was a very profitable liaison, because we learned from each other. We had a chance to discuss things. If

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\*E.H. Lennette, E.R. Rickard, G.K. Hirst and F.L. Horsfall, Jr.  
"The diverse etiology of epidemic influenza." Pub. Hlth. Rep. 56  
(1941):1777-1778.

Lennette: you were wrong, why, somebody told you about it. It's quite different from today where everybody is so polite to everybody else. In those days, if you were old enough and had experience enough to do things right and draw the right conclusions, and you didn't, you were taken apart right there in public. So these were good discussion forums, and lunchtime was the time to do these things. Then on Friday afternoons, periodically, we would have a seminar with a speaker in house or invited. Thus, several times Frank addressed us. When Wendell Stanley came up from Princeton, he talked on the chemistry of viruses, especially tobacco mosaic and influenza.

Hughes: What about contact with Rivers?

Lennette: Unless you were working in the laboratory with him, you didn't see too much of him except at lunchtime. If you wanted to go over to his lab at the [Rockefeller Institute] Hospital and talk to him, he was always available, frequently very curt or even irascible, but always available. He was a hard taskmaster. He was a good influence on virology when it was starting out, because he would stand up at a meeting and tell you where you were wrong, no matter what it was, whether it was scientific or whether it was your poor use of English. He would always take you on. That's the way things used to be here and still are done in England. He was a good influence, if you didn't take umbrage at what he said, because if you took it personally, then you'd have a real problem. But he was doing it to keep the field straight, so it would go in the right direction. He always had comments to make of some kind. Either good or bad, he always discussed the paper, so that you never got up and gave a paper and felt this was a waste of time because nobody had received it very well. So the younger people, though he was a tough taskmaster, thought he was very fair, and of course highly respected by everybody.

#### Debate over the Nature of the Virus

Hughes: Can you say something also about the concept of the virus at this particular time, in the very late 1930s, early 1940s? What did you think these infectious agents were?

Lennette: Nobody really knew how to classify a virus at that time. The information we had was that a virus fell somewhere between bacteria and rickettsiae. That was not a sharp demarcation, because there are bacteria which cannot be grown in lifeless media. Hansen's bacillus was one that you couldn't grow in tissue

Lennette: culture, and a few others grow with difficulty. And then you had the rickettsiae, which also demand living cells and can't be grown artificially. But yet they are different, because they divide by binary fission, right in half, whereas viruses don't replicate that way.

We didn't know how viruses replicated. They didn't divide in half; we knew that much. So there was some question as to what this might represent. Is this a component of the cell to begin with? Is this a piece of a broken-off gene that with evolutionary time became a normal inhabitant of the cell? Was it a part of a gene which is transmitted and has infectious properties? We weren't quite sure. It was thought it might be a piece of the gene. Well, that's the current view today: it's a piece of RNA or DNA which has been sloughed off or incorporated into a gene sequence, and thus has been left in the cell. Generally it's silent, but it may flare up and produce infection. So this was pretty much in limbo.

I would like to bring in the book by [Clennel E.] van Rooyen and [Andrew J.] Rhodes\* and have you take a look at that, because they listed four or five possibilities of what a virus might be. The only true one was that it might be a piece of the genetic apparatus

Hughes: Do you remember if Stanley's work on the crystallization of tobacco mosaic virus--that was in 1935--had any impact on how people thought about the virus? It doesn't go along with the old microbial view.

Lennette: No, but eventually it did. At the time it didn't. It didn't because people just refused to believe it. They felt that the crystals that Wendell Stanley had produced represented a contaminant, let's say, of the cells or the tissue in which the virus just happened to be enveloped. So the work was criticized on that basis. But eventually, as biochemistry progressed, and the purification of these materials increased, this went by the boards, and he was proven to be right. I don't recall exactly what and how he did it, but he could manipulate these crystals, take them apart and show they were not infectious, but when he put the pieces together again you had a virus.

Hughes: Was he given a rough time in the beginning?

Lennette: He was, because, you see, this was so unorthodox that it just wasn't accepted, and he had to find explanations for all of these things.

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\*C.E. van Rooyen and A.J. Rhodes. Virus Diseases of Man. London: Oxford University Press, 1940.

Hughes: Also, he was a chemist, and most of the virologists in those days were...

Lennette: M.D.s. Well, bacteriology, too, the same thing. They were M.D.s primarily because this was the research degree. The Rockefeller Institute [in the preWorld War II years] was full of M.D.s, and [later] eventually the Ph.D.s came in. In retrospect, that in itself lost us something, too.

I attended a meeting at NIH a few years back. We were discussing programs, and the president of the American Federation of Clinical Research presented some data--this was to the top brass of NIH and also of Health, Education, and Welfare--and showed slides where the number of physicians within the federation was decreasing over the years, and the number of Ph.D.s was increasing. The great preponderance of the research in the biomedical field today is done by people with a Ph.D., and very few with an M.D., for various reasons. First of all, the M.D. doesn't have the kind of academic training--he doesn't know how to write a grant application to begin with, so he's got two strikes right there. And then the next time around he's perhaps naive in how he explains what he wants to do, whereas his academic colleague with a Ph.D. is much more sophisticated in research and more polished, so he writes a good application. So the M.D.s have been losing out, which is unfortunate, because the Ph.D.s as a whole don't have the same outlook on medicine as does an M.D. When you get into a laboratory, you're going to have a very constricted view of life, because you're interested in one aspect of virology or immunology, whatever it might be, whereas a physician generally, because of his training, takes a broader view. I know that to be true. Of course I could argue on either side.

Lennette: So it took some time for Stanley's work to be accepted. It was a whole new concept. Now about this time, chemists and physicists were working on bacteriophage, and again, the people in medical virology pooh-pooed the work on bacteriophage: why are you working on something entirely foreign to virology and medicine? It has nothing to do with medicine as applied to man or animals. Yet out of that came the foundations of molecular biology. This is back in the late forties, early fifties. And that's what set things off. Here it wasn't the M.D.s who produced this; it was the biochemists and geneticists.

## Encephalitis and Yellow Fever Studies in Brazil, 1941-1944

Hughes: Brazil. Are we ready?

Lennette: Yes.

Hughes: Could you tell me how you got there?

Lennette: Well, I was in New York when the foundation, for its own reasons, (orientation toward agriculture and the social sciences), decided that our team should be broken up and staff sent their various ways on other problems. This was just before we entered the war. George Hirst had come in, and would be the logical person to take over the influenza area. Eventually when Frank Horsfall left to rejoin the institute as director of the hospital, Hirst took over. He ran the influenza laboratory until he left to become director of the New York Public Health Research Institute, a shop of his own. So George got pretty much of the influenza work, and I was assigned to Brazil to work on yellow fever.

Hughes: Was there any particular reason to send you?

Lennette: No, but it's just like the military. By Rockefeller Foundation edict, you were an expert. So I was an expert on yellow fever. Never worked on it. [laughter] Well, it wasn't quite that bad. You had to have a few marbles anyway.

Hughes: You were a neighbor of Max Theiler.

Lennette: Yes. [laughter] So I proceeded to Rio de Janeiro. John Fox, who was a classmate of mine at the University of Chicago, was already there, and was working on yellow fever in the laboratory and also out in the field. So when I arrived, I began to work on neurotropic viruses, only because the vaccine in several episodes had been tied in with outbreaks of encephalitic disease. The question was, is the vaccine actually producing encephalitis? Well, it turned out that we were dealing with eastern equine virus. I had had several field experiences there, and one of there was fairly extensive. We got the virus out of a horse brain.

Hughes: Several of the papers mention Venezuelan equine. Is that the same as eastern equine?

Lennette: No, there are three so-called encephalitis viruses. There's western equine. That's a foolish thing to do, to name a virus or any agent after a place, because it then never appears there subsequently. For example, St. Louis encephalitis: it hardly

Lennette: ever appears in St. Louis. So western equine was mentioned because it occurs here in the western states. And eastern equine along the eastern seaboard, down through Florida. And then Venezuelan, which appeared first in Venezuela, but has all of that northern area, in Columbia and so on, and has even been found in Florida. So there are three distinct viruses that produce pretty much the same clinical symptoms in man. We know a lot about Venezuelan today. It isn't always a fatal disease. It acts like influenza virus; it produces a respiratory sort of disease and then disappears.

So I was working on Venezuelan equine virus, mostly because we didn't know what we were dealing with in Brazil, whether it was eastern, western, or Venezuelan encephalitis. Venezuelan virus was discovered in Venezuela by several investigators there. It had been studied in the U.S. very perfunctorily. We thought if we had an encephalitis virus, we ought to have all three agents here. In part that did us in, too, because we used in the laboratory... Mind you, that's a very potent virus. We had been inoculating mice with Venezuelan equine and with western or St. Louis to follow transmission of the virus from mother to offspring. The mothers would cannibalize the young if you didn't handle them properly, and then the blood, the tissue, would be all in the sawdust, in the shavings.

We used a standard technique. We put on gloves, and used a long pair of forceps to stir around in all this stuff, looking for how many animals had died off. We created aerosols of contaminated dust and we probably brought down the whole research team with Venezuelan equine. We didn't know what the disease was that occurred in our group, but several of the technicians in the laboratory got quite ill. Elena Perlowagora, a Polish physician who was working with us, got awfully ill with headaches, colds...

Hughes: And you did yourself, I understand.

Lennette: Yes, they wrote me off. They were ready to bury me, after Austin Kerr came out to see me. I was very, very ill. And then Hilary Koprowski came down with the disease. By that time it dawned on us there was something strange and wrong, and it was probably this virus we were working with that caused these symptoms. So I wrote up our experience.\* It was virtually one of the first instances of transmission of an arthropod-borne virus via the air.

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\*Edwin H. Lennette and Hilary Koprowski. "Human infection with Venezuelan equine encephalitis virus." J.A.M.A. 123 (1943): 1088-1095.

Lennette: We were preempted by Jordi Casals in the New York laboratory. He was also a Rockefeller Foundation staff member who came from that old unit of Peter Olitsky's. Jordi showed that in one case infection with V.E.E. must have been a respiratory affair, because he recovered the virus from throat washings, which is what we did, too. We thought we were dealing with flu originally, except it was awfully severe. So we recovered the virus from these patients. I think ours was the second paper, but it had enough patients in it to make it impressive. This virus was nothing to fool around with--we had a lot of respect for it. This was a demonstration that these viruses can be infective by a role other than mosquito transmission.

Hughes: How did you change your technique after that? I hope you didn't continue to root around.

Lennette: No, we were very careful. By that time we were all immune. We could have been as careless as we wanted. [laughter] But we had to think of people in the hallways and down in the offices. No, we didn't stir around looking for animals in the cages. We tried to put layers of paper over the shavings so that the excrement would be absorbed, and we capped the tops of the cages.

That's the standard technique now in this laboratory, those caps. We became pretty leery about lab infections. That's why this laboratory was designed and built the way it is with many physical devices to protect against infection of personnel, a wholly contained laboratory, as it were.

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My complaint against M.D.s going into research in microbiology was that they were so poorly trained they were always a hazard to everybody, whereas a Ph.D. in academia was trained by the preceptor system and had a good grasp of sterile techniques and safety precautions. Well, recently that has turned out not to be quite so. But it was true in the Rockefeller Foundation. We were very rigorously taught how to handle these materials, because there was a potential threat every day either of a severe infection or death. We developed a lot of techniques that were not used elsewhere.

So when I built this laboratory here in Berkeley in 1955--it was opened in '55--we had all the latest physical protection devices. We had UV [ultraviolet] lamps to sterilize the air coming in, and air incinerators to sterilize the air going out of the highly infected rooms. We had air locks, where you had to close one door before you could open the second one in the lab, and negative pressure on the laboratory side so that if you did perchance open both doors, air would blow from the hallways into the lab, not vice versa.

Lennette: All of a sudden, in the seventies, this is rediscovered by the recombinant DNA people, who were chemists and geneticists and who knew nothing about microbiological techniques, and thus made big mistakes. We said, "Well, what else is new?" Our precautions are such that we could run a laboratory such as this in a building such as this. We used to have eight hundred, eleven hundred people in this building--not all of them in the laboratory--and so you have to think of all the eight hundred people outside the labs who are being potentially exposed. We were somewhat better trained than most of the doctoral level people, including the Ph.D.s, and I think that's why we always had such a good safety record. We haven't had many lab technicians that were ill, except for this one episode, which was enough.

Hughes: How long had the Rockefeller Foundation been in Brazil?

Lennette: I don't know exactly how many years, but it must have been at least ten years.

Hughes: Did Theiler ever go down there?

Lennette: No. He probably visited, but Max never worked in Brazil. He was not a member of the team. The moving spirit of that was Fred Soper, who was an epidemiologist.

Well, to go back to the early days, I think I mentioned Paul Hudson and Adrian Stokes and Johannes Bauer formed a team that recovered yellow fever virus from this native named Asibi. They recovered it in rhesus monkeys which had been imported, and had never been exposed to yellow fever, and therefore were susceptible. In succeeding years, a great deal was learned about the virus, and it was thought we knew everything about its transmission via Aedes aegypti, and so on. The control of yellow fever is simple, get rid of all the Aedes mosquitoes around town, because you didn't find them out in the jungle; you found them in the cities around houses. As a matter of fact, health authorities were able to clean up all the infected seaports, so yellow fever virtually disappeared. You didn't see much of it till it was discovered in the interior of Brazil. It was called sylvan or jungle yellow fever, and that changed the whole picture, because now the control of yellow fever became quite a different proposition.

Well, it's pretty hopeless out in the jungle. How are you going to control all the wild animals, all the fauna, as well as man? Man you can vaccinate, but how about the fauna? At least I don't know how you would do it. So it seemed that to find out what was going on in the jungle, you used susceptible

Lennette: animals that you put out to see if they became infected. Through such techniques they discovered what species of mosquito in the wild outside of the cities transmit yellow fever, and then they could find out how much yellow fever occurs in man.

Outbreaks would occur, and an investigator would go in there and usually the mayor of the village or hamlet would order what is called a viscerotomy. This by decree law meant that any individual who died of an acute febrile disease of less than ten days duration should have a piece of his liver removed and sent to the laboratory for examination for the presence of so-called Councilman bodies seen in hepatic yellow fever lesions. This way you could tell where yellow fever was occurring. However, since people are greedy, we ended up getting pig livers and cow livers and all kinds of livers. But that didn't last too long because usually the mayor of the town was the person who had to order the viscerotomy, because he knew what was going on in his own purview. But these people would sneak these other things in because they got twenty-five cents, as I recall, for each specimen. They were amazed when the pathology lab in Rio would send back a report saying this is pig liver or this is monkey liver or whatever, because they had distinguishable structures, so these people became believers pretty fast. That's how we kept track of that.

Viscerotomy was invented by Rickard and some of the other people there at the time. The effort was focused on yellow fever. How can you eliminate it? Well, of course, we didn't get any real control of jungle yellow fever by trying to control vectors. We used yellow fever vaccine.

Vaccines were being used on a broad scale. The vaccine was made primarily in Rio, but sometimes we brought it in from the foundation lab in Bogota, Colombia. We had occasional episodes of encephalitis or of jaundice, especially jaundice, following immunization of a populace. Later it was found that the yellow fever vaccine was producing the jaundice because of the serum which was used. This antedates me because I was not in Brazil when all this work was being done by John Fox, Enrique Penna, and others, and they finally got definite evidence that the serum was causing it. Human serum was used as a stabilizer for the virus. The virus is grown in chick embryos. The embryos are ground up and the supernatant fluid taken off as a vaccine. The serum was added to stabilize the virus so that its activity would last more than just a few hours, and then it was dessicated in ampoules. This is what we used in the field. Well, on occasion we got outbreaks of hepatitis. There was no way to prove that this came from the vaccine short of putting it into volunteers.

Hughes: What was the participation of the Brazilians in the research that was going on in Rio?

Lennette: They were very heavily involved, because the Rockefeller Foundation had a written agreement with the Ministry of Health of the United States of Brazil. Under the agreement, the foundation supplied the wherewithal, the money, and what you might call the consulting staff, because there were only six Americans. The rest of the staff was all Brazilians, physicians o as well as technical staff. So we were probably half a dozen Americans mixed in with a couple hundred Brazilians.

Hughes: Were they fairly well trained?

Lennette: Yes, they were pretty well trained. Well, you had to be competent to work with Fred Soper, as far as the physicians were concerned. The lab techs were trained on the grounds. Most of them were not college graduates. They were just trained by the doctors. Soper was quite a taskmaster. These young scientists would come down from New York, and he would just push them hard. He was a real martinet, and you survived or you didn't. If you couldn't take all of his pressures, you just ended up frustrated and went back to New York. If you could stand it for a while it was all right, and you got Soper's support and backing.

Well, as an example, I was in Rio only a few weeks when he sent me out into the back country, into the field. Here I am, newly arrived. All I know in Portuguese is "yes" and "no." And my wife and child are here in Rio. They've got to get along as best they can with no knowledge of the language either. So he sent me off with a person who was non-English speaking, a lab tech who later on worked for me. We took off for a place called Guanhaes up in the interior of the state of Minas Gerais. This was just before World War II, and the state was overrun with Japanese buying up all kinds of minerals. We took a night train to Belo Horizonte, our jumping-off place. As the crow flies, you'd get there in probably a few hours. But the way the train went, it took most of a night. It just wound through all these hills to Belo, which is why the English were accused of building this railroad by the mile rather than by a direct route. We arrived at Belo in the morning, where the Yellow Fever Service car met us and the local yellow fever officer briefed us on the events in the Guanhaes area.

Hughes: Was there an outbreak of yellow fever?

Lennette: No, but there was some encephalitis there, and that's why I was sent in. The car picked us up, and we drove quite some distance inland and got to the very end of the road, then took off cross-country for a few miles and entered this little village. This was either cross-country or maybe it was just an awful rough road. Anyway, we arrived in this little village and stayed at the only pension there. Of course I spoke no Portuguese, so I had a terrible time. This kid spoke no English. We stayed at this place, and I had to sort of sign language everything I wanted to do for the first week or so. Almost froze to death, it was so cold up there at night. It was up in the mountains, you see. The bed had a little thin mattress on it. The lights went out in all the houses at ten o'clock at night. The pension rooms had one bare bulb hanging from the ceiling, and the local power plant was shut down at ten o'clock every night. It was owned by the mayor of the town, as I recall. There was nothing you could do. You couldn't read, so you just went to bed, but you couldn't sleep because it was so bitter cold.

Well, we went out in the field a few times. We found out from some of the local people where some of the patients lived. I got some blood from them, but I wanted to get some blood from the local horses also. I didn't know how to handle it. Just about that time--I had been there four or five days--a Yellow Fever Service chap came up from Rio. He was of Polish descent. His father had come from Poland, and was a professor of surgery at the University of Parana in southern Brazil. And his son, Luty Kossobudzki, had done some of his postgraduate medical work in Warsaw, where he had learned some English. Luty arrived on the scene, and showed me how to stuff a lot of newspapers under the mattress--how to survive in the interior and in the high altitudes of the Brazilian mountains--so from that point on, I could get a little sleep.

Luty knew what I wanted, so he arranged to get some horses bled. "You've got to stop these guys, these locals, when they come into town on their horses and donkeys." He just got in touch with the mayor, and told him what we wanted to do. Saturday morning, with everybody coming into town to market day to do their purchasing and buying, he just stopped all the horses coming into town. Luty would wrestle and throw the horse on its side--we had a local vet helping us--and I would stick the needle into a neck vein and get some blood. As simple as that. You couldn't do that in this country. The chap who owned the horse was usually interested in what was going on. His horse was thrown on the ground, was bled, and he just stood there looking on, making no protest. He thought it was a rather interesting procedure, especially when we told him what we were going

Lennette: to do with the blood. So I spent about two weeks up there, and of course I lost a lot of weight, because the interior sanitation was such that it sort of threw you off your feed. That was my first exposure to Brazil and one way of life outside of a big city like Rio.

The other notable part of the expedition was that when we arrived at Guanhaes, the chauffeur took the whole engine apart out of this car. This was in front of the local church, out in the plaza; all the pieces were laid out in orderly fashion. I said, thoroughly convinced, "My heavens, we'll never get home. He'll never put this together." But these chaps were pretty well trained as mechanics, because they had to be. If you're in the interior and anything breaks down, you have to know how to repair it. You can't call the local garage a half a mile away. You've got to repair it yourself. So they were pretty good. He got it back together with no fuss.

That was my introduction. I survived that, and Soper thought maybe I would endure, so he kept me on in Brazil. He was a good teacher.

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On another field investigation, I was accompanied by Hugo Laemert, a young Brazilian physician of the National Yellow Fever Service.\* Hugo came from a German background, and his father was also a physician, practicing in Rio de Janeiro. In any case, we flew up to San Salvador, now called Bahia, in the state of Bahia. We were destined for a town named Ilheus, where several cases of central nervous system disease had been reported. To get there from Bahia involved a short trip in a small three passenger plane which flew down the coast over tree top level and then inland for a short distance where we took a dugout canoe across a lagoon or bay to the other side. Since this was primarily a quick medical and epidemiological investigation, we did not collect any clinical or field materials, but merely prepared a report on what we had found. It is of interest that a year or so later, a field crew into that area collected clinical specimens from patients observed at that time and also from various arthropods and mammals. A virus was isolated from mosquitoes and named Ilheus virus by Drs. Laemert and Enrique Penna who supervised the field and laboratory effort.

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\*Dr. Lennette wrote the following two stories of field trips in Brazil, after the interviews were completed.

Lennette: On an earlier instance, Hugo Laemert and I were sent to investigate the possible occurrence of yellow fever in a small hamlet named Santa Maria the Caucai some distance north and east of Guanhaes and Governador Valladares, the area of an earlier investigation by me concerning the occurrence of encephalitis following the presumed use of yellow fever vaccine.

Hugo and I went by train to Belo Horizonte, the capital of the state of Minas Gerais, and then by Yellow Fever Service automobile as close to Santa Maria as we could get although we had some distance to go. We were met by a physician from the Yellow Fever Service who was to be our guide and assistant. Through the good offices of the mayor of this small town where we met, we were provided with horses and the three of us set off for Santa Maria some three to four hours distance by horseback. (I had not been astride a horse for years and the ride through Santa Maria and back a day or two later rendered me hors de combat for several days after my return.)

I noticed that the local physician, who was wearing a white linen suit and a panama hat, carried a huge pistol which stood out because the holster was black against his white suit. I didn't feel a pistol was necessary, even in this relatively sparsely settled area, so I asked what purpose it was to serve. The answer was that the forest in which we were riding was home to jaguars and it was always possible that one might be encountered. To which I replied that a pistol hardly seemed a very effective weapon and a rifle would be the preferred instrument of defense. It later came out that he had been investigating an outbreak of suspected yellow fever in the Santa Maria area and had hoped to get a liver specimen of a child who died after an illness of several days which was thought might be yellow fever. According to law, any individual dying of an unknown fever of less than 10 days' duration should be subjected to a viscerotomy and the liver specimen sent to the laboratory in Rio de Janeiro. The family was opposed to his taking a specimen, and since he had no viscerotome, he used a razor blade to make a small incision and to get a small block of liver tissue. Remember, now, this was in the interior of Brazil and he was dealing with a relatively backward populace with attitudes such as those encountered in our own Appalachia. His procedure, despite familial opposition lead to what might be called a feud, and he became persona non grata in the Santa Maria area and might well be done in.

The moral of this episode is that he was more afraid of Fred Soper's punishment than he was of the villagers, and it was this fear and respect of Fred Soper, with the attendant hirings and firings, that led into the development of the Yellow Fever Service as an outstanding governmental operation with a true esprit de corps.

Hilary Koprowski

Hughes: What about Koprowski? Did he come straight from Poland?

Lennette: Hilary was a bright young man, just out of medical school, who was trained in biochemistry. He had spent a year or two in Dublin in biochemistry as a postdoctoral fellow. He got back to Europe just about the time the war broke out. Hitler's armies were all over western Europe. Hilary had left Poland with his family. His father, an officer in the Polish army, went to England. Hilary, his mother, and his wife got as far as Paris, where their first son, Claude, was born. They now had a baby to contend with, and they wanted to come to the States, but when they got to Lisbon, the pressure was so great with the German armies behind, that they took the first vessel available, which happened to go to Brazil--to Rio, as I recall. Anyway, they ended up in Rio. Of course, like many people with no roots, Hilary had to find his way--he had to learn the language, which was no problem for him because he's a very good linguist, and also a fine pianist with a diploma from the Rome Conservatory of Music. He got a position with, I think, a local brewery doing biochemical tests; of course, just a stopgap.

One day, as I recall, he was walking down the streets in Rio, he ran into Luty Kossobudzki. Luty had been in the graduate medical school in Warsaw when Hilary was there, so they knew each other. Of course, there was the usual exchange of pleasant-ries. Luty said, "You're not working up to your capabilities. You want a better job than that. Why don't you contact the Yellow Fever Service? They are looking for staff members."

We were always glad to get new people. Hilary came out to see us at the lab. I was upstairs in the laboratory when Hilary came, so he talked to John Fox, who was the temporary number two administrator when Austin Kerr, the number two man was away.\* Austin was out of the country at the time. John was quite impressed with this young man. He said, "Why don't you go upstairs and see Lennette. He's in the laboratory. He's a virologist." So he came up to my lab to see me. I was leaving for Guanhaes, which I mentioned earlier, so I didn't have much time to talk to him. I was in a hurry, and we had a cursory, perfunctory discussion. I gave him a whole big stack of reprints on medical virology. "You read all this stuff. I'll be back here in three weeks, and I'll quiz you on it." When I came back in three weeks, Hilary had read all the papers. It was very impressive, what he had garnered out off all this. You know, this was a strange field to him; he was a biochemist, not a microbiologist. He and I then became a team, and worked very closely together for the time I was in Rio. This was in 1941. I left there in '44, so we were together for about three years.

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\*Fred Soper was the number one administrator.

- Lennette: The other person in my group was Alina Perlowagora, a Polish emigré, who also was very good. But Hilary obviously was a very, very outstanding student. When he later came up to the States, he made quite a career for himself, an outstanding scientist.
- Hughes: There were two papers that you wrote when you were in Brazil, which I would like to hear about. One of them was published in 1943, and is a survey of viral research, which I found very interesting.\* Some of this we've discussed before. One thing that you mentioned that caught my attention, you said that plant viruses were more intensively studied at that time than animal viruses. Was that just a matter of ease and convenience?
- Lennette: No, I think it was because of the economic aspects. I don't recall what's in that paper, but I think that was our reason. There was a lot of work being done in the thirties on plant viruses in England, at the Rothamsted Experimental Station. Quite a few of the Europeans and many Americans went to Rothamsted to get training in plant virology.
- Hughes: That's [Frederick C.] Bawden and that group?
- Lennette: Yes, Bawden and [Norman W.] Pirie. A very fine institution. A great deal of research was done there, whereas the work on viruses in human and veterinary medicine was kind of catch as catch can, and not as organized. Of course, it's a lot more expensive, because you have animals to nourish, feed, breed, etc.
- Hughes: Do you recall how much electron microscopy was being used at that point?
- Lennette: Not very much, because the electron microscope, as I recall, was introduced about 1933-34 by the Germans, but there was no great incentive to use it. A remark was once made, "It's all well and good, but what point is there in magnifying a banana a hundred thousand times?" You got a huge banana, but you couldn't see much detail--there was no resolution. So it wasn't until they proved able to bring in some resolution that the scope became valuable, and this was in the fifties probably. Today, of course, it's a routinely used instrument, if you have one. At that time it wasn't used very much at all.

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\*Edwin H. Lennette. "Recent advances in viruses. A brief survey of recent work on viruses and virus diseases." Science 98 (1943):415-423.

## Interferon

- Hughes: Then there was another paper\*--it was actually three years later, in 1946, and Koprowski was a coauthor--on interference between viruses in tissue culture, which interested me for what we now know about interferon, which of course wasn't called that at that stage.
- Lennette: Well, again there were a number of people working on this. We got to the stage where we couldn't go any further. We didn't have the tools or methods. This was 1946, and we didn't have the biochemical or the immunological approaches, which were later developments. But we knew that in these cell cultures something appeared in the infected culture which protected against infection by a second virus. In a yellow fever culture, the cells were protected against infection with influenza virus, and so on. I don't recall all the combinations we used, but there was certainly something which interfered with the growth of the second virus that was added. We didn't know what the factor was, and we couldn't get it out, isolate it. We tried a few very naive chemical approaches, and nothing happened.
- Hughes: This seems to me to be getting into fairly basic research.
- Lennette: It was.
- Hughes: Were you given virtually free rein by the International Health Division?
- Lennette: Yes. There was never any criticism of anything we wanted to do, provided within reason we met the objectives of the division. After all, this was the International Health Division; you couldn't go out and do something which was extraterrestrial. [laughter] But as long as you stayed within reasonable bounds, nobody ever criticized you. As a matter of fact, you got good support. I can't recall a single instance where I was told not to do something.
- Hughes: Did this paper on interference make much of a wave?

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\*Edwin H. Lennette and Hilary Koprowski. "Interference between viruses in tissue culture." J. Exp. Med. 83 (1946):195-219.

Lennette: No. As a matter of fact, the interferon phenomenon goes way back, even to primitive people, e.g. Africa. They knew if you had certain diseases you couldn't get other ones. That's a housewife's observation, a myth, as it were. But that nonetheless was true. Then in the laboratory this was shown by [George M.] Findlay and F.O. MacCallum using yellow fever virus. It had been described by the British, and then later on a number of other viruses were used to show this is a real phenomenon. We were using tissue culture because we felt we would have some chance of success in using a relatively clear fluid to extract it chemically. If you have a mishmash of mouse brains, for example, it's a terrible starting material, and we never got very far in animal experiments.

Hughes: So that was technique-limited.

Lennette: A technique limitation. Well, one investigator once said that Lennette and Koprowski discovered interferon but they were too dumb to know it. That isn't true. We knew there was something in the cultures. We couldn't isolate it and so we didn't know what it was. We didn't discover a new drug. We don't take any credit for that. The credit goes to Isaacs and Lindenmann.\*

#### The Use of Suckling Mice in Viral Assays

Lennette: We had another two papers which never received the recognition they should have. One of them is the susceptibility of infant mice of different ages to different viruses.\*\* We used eight or nine different viruses: herpes, St. Louis, western equine, Venezuelan, LCM [lymphocytic choriomeningitis]. We used mice of different ages and showed that the mice were susceptible to some of these viruses and not to others, that resistance to diseases increased with age.

Hughes: That was with Koprowski, too?

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\*A. Isaacs and J. Lindenmann. "Virus interference. I. The interferon." Proc. R. Soc. 147, B, (1957):258-267.

\*\*Edwin H. Lennette and Hilary Koprowski. "Influence of age in the susceptibility of mice to infection with certain neurotropic viruses." J. Immunol. 49 (1944):175-191.

Lennette: With Koprowski. The other paper was the use of this technique for doing antibody assaying.\* Now two things happened. The first was when Hilary presented some of his data at a meeting after he came up to the United States. He presented this about 1946 or '47 at a meeting of the American Association for the Advancement of Science in Cleveland, and the work was very roundly criticized. What laboratory is going to use suckling mice one or two or three days of age? That's preposterous. Nobody's got that kind of money. Nobody's got the space to breed all these animals. So all this work was sort of pooh-poohed.

The second is the whole thing had to be rediscovered just a few years back. I was amazed to learn less than a year ago from a very prominent investigator of the arbovirus group that he was unaware of these papers, mind you, unaware of them although he used the methods. The point is that here was a tool that had to be rediscovered. Secondly, the idea that nobody could use these techniques was wrong, because after all, when I came to Berkeley from Rio, we began to use baby mice. Coxsackie viruses were discovered through the use of baby mice by [Gilbert] Dalldorf in Valhalla, New York. These are very important viruses. We use baby mice routinely in this laboratory. We at one time had a colony of ten thousand mice here. They were used for breeding, producing young mice.

The crux of the whole thing is that in some cases, like the coxsackie viruses, you can't use older mice. It's so important that you can always tell if a breeder is fobbing off older mice on you because the mice won't come down with illness. There were dealers like that in the early days. Instead of giving us a two-day mouse, they'd give us a three-day or older mouse, and nothing would happen to the mice used in a test.

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\*Edwin H. Lennette and Hilary Koprowski. "Neutralization tests with certain neurotropic viruses. A comparison of sensitivity of the extraneural and intracerebral routes of inoculation for the detection of antibodies." J. Immunol. 49 (1944):375-385.

The Rockefeller Foundation Laboratories at the California State  
Department of Public Health, 1944-1946

Lennette: I had been stationed in Brazil, working on yellow fever and the encephalitis viruses.\* My tour of duty was essentially complete, so I was assigned here to Berkeley in 1944 by the International Health Division of the Rockefeller Foundation to work on hepatitis. Hepatitis was important because of the many cases which followed the use of yellow fever vaccine in army recruits. I was also to establish a viral diagnostic laboratory by adapting current methods or devising new ones to provide diagnostic assistance to the medical and public health people. Such a service did not exist--the only viral diagnostic laboratory in the country was that established by Joseph Smadel at Walter Reed Army Institute for Medical Research when he left the Rockefeller Institute as a commissioned officer in the Army Medical Corps. In effect, the Berkeley laboratory was the first civilian viral diagnostic laboratory, and as such, together with Joe Smadel's laboratory, pioneered much of the field.

Monroe Eaton and the Eaton Agent

Lennette: During the time I was here, Monroe Eaton was working in the laboratory, too. He was not an administrator; he actually worked in the lab. He hated administration. He was working on what came to be known as the Eaton agent, isolated from patients with atypical pneumonia.\*\*

He had spent some time in the New York laboratory working on influenza, so all of his thinking was pretty much colored by influenza virus work. He arrived on the scene in Berkeley in 1938. The lab had just been opened. He was working on flu and any other respiratory diseases that happened to occur.

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\*Dr. Lennette wrote this paragraph after the interviews were completed.

\*\*M.D. Eaton, G. Meiklejohn, W. Van Herick, and J. C. Talbot. "Infectious agent from cases of atypical pneumonia apparently transmissible to cotton rats." Science 96 (1942):518-519.

Lennette: During the war the Kaiser people had built big shipyards at Richmond, and every weekend there would be dozens, I guess, of cases of atypical pneumonia in the yard workers.\* Cases just filled the hospital beds, so Monroe had a wealth of clinical material to work with, and out of all this massive amount of material, he recovered an agent which produced pneumonia in cotton rats and hamsters.

This was a difficult agent to work with, because you couldn't passage the virus in animals continuously the way you do with most agents. If you make three or four passages in a cotton rat or in a hamster, you would end up with hamster pneumonia virus or a cotton rat pneumonia virus. It's really a dead end, so you had to go from the animal into the embryonated egg. Now you've got other problems. You get into the egg, and about the only part of the chick that had any virus in it was the trachea. In a ten, eleven, twelve day old egg, the trachea is a little bitty thing, so you need a fair number of eggs to get any kind of a workable amount of virus.

Well, anyway, he was able to produce pneumonia in animals with the chick material. He scored the pneumonic lesions by one-plus, two-plus, three-plus and four-plus. When other people tried to repeat his work, they couldn't get any four-pluses, because the scale he was using was based on the scale that was used in influenza. One-plus meant one fourth of the lung. Two was half of the lung. Four-plus was complete consolidation. But with the Eaton agent, this was just a matter of how he scored it, using different and somewhat subjective criteria.

Gordon Meiklejohn, who just recently retired as chairman of the department of medicine at the University of Colorado, was working with him, and they had something infectious going in animals. I wasn't deeply interested in that problem, and although I wasn't working on it, I was exposed to it. I couldn't go through the laboratory without hearing something about it, so I developed sort of an interest in what these two chaps were doing.

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\*Dr. Morris Collen discusses his work on pneumonia in Morris F. Collen: The History of the Kaiser Permanente Medical Care Program, an oral history interview conducted in 1986, Regional Oral History Office, The Bancroft Library, University of California, Berkeley.

Lennette: It seems nobody in the East could repeat what Eaton was doing. George Hirst couldn't repeat it. Frank Horsfall couldn't repeat it. Dick Mirick couldn't repeat it. Nobody. So, therefore, what's going in that Berkeley laboratory? They're having pipe dreams. Now these were the top people in the viral respiratory disease field, and if they can't repeat the experiments, there's something strange going on, something's amiss, wrong. Well, they weren't following his techniques, his methods, his procedures, and were using a different scoring method. Hugh Smith was in the New York office, the associate director of the IHD. Hugh came out here to see what was going on. So they were all set to pull Eaton out and send him back East so that he could work on this agent and show them what was going on, and then maybe put him on some other project. I fought them off. I just wouldn't hear of it. I said, "He's got something there, why don't you give him a chance to really work this thing over?"

He subsequently left the foundation about '46 to go to Harvard as professor of microbiology, and then the whole research project fell apart. He had some small experiments that he did--he was now a teacher and he had committees to serve on--so the time he had for research was very small compared to a full-time eight hour a day research job. In the interim, some of this work was being repeated in England. And then Barry Marmion, who was in England, and Robert M. Chanock of the NIH, both showed almost simultaneously that what Eaton was dealing with was a mycoplasma. If you go back to Eaton's first publications in the Journal of Experimental Medicine, you will see some beautiful electron micrographs as well as pathologic sections, and you can see the mycoplasma. Eaton, however, thought it was an extraneous organism that's present in the chick embryo, and didn't give it any credence that it could be involved in human pneumonia. For a long time, nobody knew what he was talking about, so they called it the Eaton agent.

For years there was very little in the American literature about the Eaton agent. Much of it was in the British literature, which is a commentary in itself. Anyway, the National Institute of Allergy and Infectious Disease called a meeting at the National Institutes of Health to discuss the properties of the Eaton agent and its role in atypical pneumonia. It was held in the clinical center which has a big auditorium; it seats a thousand people, maybe more. It was nice to have Eaton invited to this meeting, because all through the three days I don't think he uttered a word. He just sat there smoking his pipe and grinning. Everything he had said had proved out right. He was completely vindicated. [laughter]

Lennette: This related to what we were doing at Fort Ord, California. About that time aureomycin, the first wide spectrum antibiotic, had come in, and penicillin was also available. We were treating these atypical pneumonia patients with aureomycin, and with penicillin as sort of a control. Anyway, some years the patients responded to aureomycin therapy. Other years aureomycin wouldn't even touch the disease. Well, some of the people back East in infectious disease said, "Well, you give them penicillin, you give them aureomycin, all you do is give them an antipyretic. You're not accomplishing anything." Whereas our criterion was you got a pretty sick GI here in bed. He's very ill, and you start giving him antibiotic therapy and pretty soon he's ready to eat a steak, but the real criterion is when he wants a comic book. If he wants a comic book, he's recovered. [laughter]

In any case, we were able to show that the reason that they'd respond was because the atypical pneumonia was due to the Eaton agent. At other times it was due to an adenovirus, and the adenovirus infections didn't respond. That made some of the people back East see that we were on the right track. So we too were vindicated, and with Eaton were part of the scientific community again.

#### Encephalitis Studies

Hughes: Well, since we're on that period, let's finish with your first visit to California. I know there was one paper on the isolation of St. Louis encephalitis virus in a human in California.\*

Lennette: That's another commentary on the inadequacy of our methods.

When I came to Berkeley, my first technical assistant was Carol Shon. She was a fiesty little character, outspoken, quick-triggered. Carol and I got along fine. We were working on two viruses, the St. Louis and western encephalitis agents. You see, you get various threads through all of this. We were working on these two viruses because a chap by the name of C.H. Huang at Columbia University, working with Jungeblut, had found that if

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\*Edwin H. Lennette. "Isolation of St. Louis encephalitis virus from a fatal human case in California." Proc. Soc. Exp. Biol. Med. 61 (1946):206-210.

Lennette: you put St. Louis or western equine virus into tissue cultures... Now in those days, tissue culture wasn't what it is today. Tissue culture at that time was: you took a chick embryo and minced it fine with scissors. You placed these pieces of tissue in Ringer's solution or Tyrode's solution in a small flask, and that was your culture. These cells would settle down at the bottom of the flask and would grow out as a layer. Very poorly controlled conditions.

Huang had found that if you introduce western equine virus or St. Louis virus into such cultures, they would grow. You had a phenol red indicator in the flask that as the cells grew and multiplied, they would produce a metabolite that would change the color of the phenol red to yellow because of the acid accumulation. On the other hand, if the virus killed off the cells, there would be no metabolic products, of course, and the phenol red would stay red.

We were trying this and getting nowhere. In any individual patient we could not make a diagnosis. En masse, statistically, yes, we could see that the method had promise, but we did not pursue it further.

To return to the patient, this individual was walking along the highway in the Stockton area, as I recall, and collapsed and was taken either to the jail or to the hospital. The sheriff's office thought he was inebriated, so I think he probably ended up in the local jail, where he died over the weekend. An autopsy was done because this was an unattended patient, and the brain tissue sent to the Berkeley lab. So Carol and I put it into some of these tissue cultures, more cogently into baby mice, and got a virus out.

The next question was, what is this virus? Well, you know, we fooled around with that virus for almost six months before we got it identified for the very simple fact--and this was one of the salutary lessons--that a virus freshly isolated from man does not behave like a virus which has been around a laboratory for a long time and has been passaged repeatedly from animal to animal. A virus is comprised of an inhomogeneous group of viral particles, and when you pass it through animals, you select out those particles which will grow in that tissue--those that won't grow just get left behind--and so you end up with a highly adapted strain. So eventually we had to write the books for diagnostic virology, because we had a flood of these examples.

Lennette: Before I left St. Louis, I had written a paper\* on the behavior of St. Louis and Japanese B virus in baby mice, what the differences were and how the young mice were killed off. This agent didn't behave at all like my description. It was really Carol Shon who said, "I think it's St. Louis virus," and she was right. So she really identified it. Well, from that point on we knew that you have got to use other methods.

We found the same thing, incidentally, later on with herpes simplex virus. We saw these differences between wild and laboratory strains early, but we couldn't nail them down. We had no way to study them. This was back in the early fifties. We knew that there were differences, because we used a laboratory strain of herpes virus to test serum from patients with herpes. These sera were positive by complement fixation, but by neutralization tests they were very weakly positive. So we thought there might be strains, you know, types. Today that's well known. It's also a very important matter. So that's how we got started on the St. Louis virus.

Hughes: Is that enough about your first visit to California?

Lennette: I guess so, because I was here only those two years, and it was mostly on this encephalitis project. These kinds of things, like the encephalitis, were just by-products, just to keep me from losing my mind working on hepatitis. There was nothing that was going to emerge from that.

Hughes: You didn't actually publish on hepatitis?

Lennette: No, because there was nothing to publish on.

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\*Edwin H. Lennette. "Influence of age on susceptibility of mice to infection with certain neurotropic viruses," J. Immunol. 49 (1949):175-191.

Camp Detrick, Maryland, 1946-1947

[Interview 3: October 7, 1982]##

Hughes: You were at Camp Detrick from 1946 to 1947.\* Can you tell me how you got there and what you did when you were there?

Lennette: I was in Berkeley from September of 1944 until June of 1946. My reason for leaving California and going to Camp Detrick was in large part economic, and secondarily, I guess, an opportunity to do some other things. The Rockefeller Foundation had never been noted for being overgenerous to its staff.

Camp Detrick, as you know, was a so-called biological warfare institution during World War II. Upon the cessation of hostilities in 1945 there was some doubt and some question as to what would become of this institution, whether it should be continued due to sparring between the Soviet Union and the Western world or whether it should be devoted to other purposes.

So I took this opportunity at Detrick first of all, as I said, for the economic aspect--they gave me a much better salary than the Rockefeller Foundation, and secondarily, because of the containment issue. I could see good opportunity for research on the increasing number of arboviruses which were being recovered around the world, especially in South America and Africa. This was a field which was just developing, and I thought high security containment of these organisms, for which Detrick had established quite a reputation, would provide a possibility for research on these new and unknown viruses.

We were getting under way, but I never got into research. I was frustrated dealing with the military establishment; I was just inundated with bureaucratic red tape, continually revising budgets upward or downward, and drowning in an administrative morass. I finally decided that maybe this was not for me from the standpoint of administration. I was a bench scientist; I wanted to get back to the bench. There obviously was no opportunity for this at Camp Detrick.

You have to remember, in the context of the time, that we were trying to reorganize this institution. A lot of the people who had been there during the war years had left for other endeavors. They had other assignments, teaching, research, or whatever, so the staff was pretty well depleted, decimated. We were trying to get new staff and take off on new programs. But the administrative burdens got to the point where I was too depressed to stay.

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\*Dr. Lennette's title was chief, Medical-Veterinary Division, Chemical Corps, U.S. Army, Camp Detrick, Maryland.

III THE VIRAL AND RICKETTSIAL DISEASE LABORATORY, CALIFORNIA  
DEPARTMENT OF PUBLIC HEALTH\*

Lennette: One day I ran into Malcolm Merrill on the boardwalk in Atlantic City. I was there for a meeting of the American Public Health Association in early 1947. This was one of my low points. After working for the military, I just couldn't see that I was getting very far. Anyway, Malcolm Merrill and Harlan Halvorson, the director of the California Department of Public Health, both had wanted me to come back to Berkeley. I told them I would come back to Berkeley, which I did at the end of November, 1947.

That changed the whole flavor of things for me because I came back with the understanding that I would have a free hand to undertake whatever research I wanted to do. You must remember, my interests were not in very basic and fundamental virology; my interests were in medical virology as applied to the patient clinically, and from the immunologic and epidemiologic standpoint.

Hughes: Had the Rockefeller withdrawn at this point?

Lennette: No, Rockefeller money was still coming into the Berkeley laboratory. Monroe Eaton, though, had left, so I came back as the director of the laboratory. He'd gone on to Harvard. The foundation was still supporting the laboratory, except for my salary, which was paid by the state, although I think it perhaps came out of Rockefeller Foundation funds given as a grant to the department.

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\*Dr. Lennette was chief of the Viral and Rickettsial Disease Laboratory from 1947 to 1978.

Effective July 1, 1978, the California Department of Health was reorganized and renamed the California Department of Health Services.

Hughes: How long did the affiliation last?

Lennette: I would have to check on it, but it seems to me it was somewhere around '51 or '52. The foundation supported the salaries of the technical staff and also the purchase of equipment, supplies, and so on. They were very supportive and very helpful and that's what kept the operation going. That was done on the understanding that this laboratory, aside from being a watch station for respiratory diseases and especially influenza, about which you could do something from the standpoint of diagnosis, would try to develop diagnostic methods for virology.

### The Development of Diagnostic Virology

Lennette: At this stage of virology, there was a fair amount of research being started up after the war. There were techniques which were very simple; they were carried over from bacteriology. But there weren't enough people really interested in diagnostic virology to make it a separate field, aside from rabies, for example, which by law you had to do something about. But if you were concerned about some disease that you couldn't quite put your finger on clinically and you wanted some laboratory work done to rule in or rule out this disease, you had to choose an academic laboratory or research laboratory which happened to be working on the particular virus in which you were interested. This meant that you had to have at hand a whole list of laboratories nationwide so that you would know what specimen to send where.

Hughes: And were these labs receptive?

Lennette: No, not especially. You could sent material; they would agree to test it, but it meant it was done at their convenience and at their leisure. If they had a real busy period and they were doing a lot of testing, they didn't have room for your materials. If it came a slack period, they might put it in, and you would get an answer back in six or eight or twelve months. Well, obviously that's no good to anybody.

So what I was charged with was to try to develop--this is back in '44 actually, when I was asked to work on some of these things--better diagnostic methods.

Hughes: The foundation was asking you to do this?

Lennette: The foundation was interested in that, because the foundation had indicated to the State of California, the health department, that if better methods could be devised or worked out or improved, and eventually reach the stage where they were applicable to the smaller laboratory, then the state should take over and farm these out to these small laboratories. This then took a number of years, because when we started, as I said, in 1947, there was no place to send materials. Berkeley, I think, was the first civilian viral diagnostic laboratory, so doctors in this state eventually got the message that there was a laboratory here that was doing diagnostic work, and they would send us material.

Now this, too, represented the state of the art, because the tests that we were using were either cumbersome or protracted, so that the time element was such that the patient had either recovered or died by the time the physician got the answer. This obviously wasn't very good.

However, from the public health standpoint, it did serve a purpose, because it gave support to epidemiologic studies, so that the people would know what disease they were dealing with. (And I'll mention that later on in connection with poliomyelitis, true poliomyelitis and diseases which simulated it, and the need to differentiate.) So the major effort in research in the Virus Laboratory in Berkeley was to develop either new methods never used before or, more cogently, methods which were already existent and that were to be simplified to the point where the smaller laboratories could use them.

That was our mission for many years. We were working towards that goal, especially in the past ten years--I'd say from about 1972-73 up to the present. Things moved very fast, so much so that ten years ago Dr. Robert L. Magoffin and I--he was the assistant chief of the laboratory--felt that most of these tests could be done in the local public health laboratories or even in the larger hospitals, medical centers. So we began to slough off a lot of the work here, and some of the health departments took over; some of the large hospitals also took over some of the workload. But we didn't really make much of a dent until about five or six years ago when we firmly put down our foot and said no more of this gadding about, either fish or cut bait, that on such and such a date we're not going to do any more tests, and you'd better start looking for alternatives. This really had results, because we just refused to test materials that came in. Much of it was farmed out, then, to the local laboratories.

Lennette: What is left is a laboratory which is recognized still as the leader in the medical laboratory, diagnostic field. It was a pioneer in the development of the techniques which are applicable to many of these diseases, not necessarily development from scratch, but improvement of the techniques, their evaluation, or, as we say today, their validation, that they were accurate, and to test materials on a great scale.

For example, when Dr. [Robert J.] Huebner was working on Q fever, then later on in the cancer field, he on a number of occasions mentioned that there were only two laboratories in the United States that could do serologic tests on a grand scale. That was his own laboratory and this one in Berkeley. I mean on a big scale, thousands of specimens, because nobody else was geared up to do it.

Hughes: Let's return to the subject of your arrival in November 1947 as director of the Virus Lab at the California State Department of Public Health.

Lennette: One of the other reasons for my coming back to California was the fact that Charlie Shepherd of the Center for Disease Control, U.S. Public Health Service, had been out here in the spring of 1947 to look at what was suspected to be Q fever in southern California. He confirmed that it was Q fever. This was a matter of some interest to me, and I thought this would be the logical place to do a study on the natural history and epidemiology of the disease.

First of all, Dr. Eaton was primarily laboratory-oriented, so his emphasis was on laboratory research. My perspective was much broader. I had an interest in epidemiology, as well as an interest in the clinical aspects. Here then was a chance to do all three things, but, more cogently, was the fact that California is unique among the states because its department of health is not a centralized operation. Each county, with a few exceptions, has its own health officer, and is virtually autonomous. In any case, here you have fifty-eight counties, and the great preponderance of them have a health officer who can act as a source of basic information on the diseases in his county, and also is a means for obtaining clinical specimens from patients to study diseases; I thought this was a golden opportunity.

Hughes: You mean in other states it's much more centralized?

Lennette: For example, in New York State you'll have regional laboratories, which we don't have in California. It's either the state health laboratory in Berkeley or local county and in some cases, city. Berkeley has its own laboratory, as do San Francisco, Los Angeles, and San Diego. The other counties have laboratories of varying size, reflecting the population size. It was an opportunity to get study material. You didn't have to go out and hire a whole cohort of investigators; they were already tailor-made. It was just up to you to use the considerable resources that were available to you.

Hughes: And Eaton really hadn't done that.

Lennette: He hadn't done that because that was not his field of interest. I don't want to detract from Eaton; it was just not his interest, which lay more in teaching and laboratory research, which he did well.

So that's what brought me back to California. Now at that time the department had, so far as I know, no research grants of any kind; it had medical contracts or payments of federal funds for operating certain aspects of the department, but not for basic scientific research. So far as I know, the grant that we asked for on Q fever was the first one in the department.

Hughes: I read the publication in 1953 of a speech that you and another person, whose name I have forgotten, gave for the opening of the Virus Lab at U.C. Berkeley. There was a short history of the State Department of Public Health in that, and according to that paper, in 1946 the state legislature paid six hundred thousand dollars for a study of encephalitis, which would have been just before you came.

Lennette: That doesn't sound right, because we didn't have any encephalitis. Actually the worst major outbreak was 1952, and money was appropriated. Then in 1957 we had another outbreak and received support from the legislature.

Wendell Stanley's Virus Laboratory at the University of California

Lennette: Your mentioning the opening of the Virus Laboratory on campus is kind of interesting, too. Wendell Stanley was a Nobel laureate, honored for his work on the crystallization of viruses, more specifically the tobacco mosaic virus. He arrived here shortly after I did, coming from the Rockefeller Institute at Princeton, N.J.

Hughes: 1948.

Lennette: Yes, I was going to say at the end of 1947 or early 1948.\* Stanley came to the University of California, Berkeley campus as chairman of the department of biochemistry and director of the Virus Laboratory. Biochemistry was in one building and his Virus Laboratory was housed in the basement of the Forestry Building, which was on the western edge of the campus just a short distance above Oxford Street, and quite large.

The department of biochemistry had outgrown its space and the Virus Laboratory, of course, was housed in temporary quarters. Wendell and his staff, and especially Arthur Knight, who came with Wendell from the Rockefeller Institute at Princeton, together with others of his staff during 1948 and 1949, were deeply immersed in drawing up the plans for a new building which would house both biochemistry and the Virus Laboratory. The laboratory was to be erected at a site between Cowell Hospital and the physical sciences area, and also directly across Gayley Road from the Hearst Greek Theater, a marvelous location, physically, with Wendell's office to be in the northwestern corner of the top floor, thus providing a panoramic view of the campus and especially of the San Francisco Bay.

Sir MacFarlane Burnet arrived in Berkeley in the spring of 1951-1952--he was always commuting across the United States from Australia to Europe--to visit Stanley's laboratory. Sir Mac had lunch at my home, after which we went to Berkeley to see how the laboratory construction was progressing. The three of us--Sir Mac, Wendell Stanley, and I--inspected the entire building with respect to the various laboratories that it was to house, and finally terminated our tour on the roof where the green

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\*Dr. Lennette wrote the following section on Stanley's Virus Laboratory after the interviews were completed.

Lennette: houses were to be located for growing plants for plant virus research. As I mentioned, the view from this elevation was impressive, a sweeping panorama of the bay. Wendell was quite happy with the space that the university provided in the new facility, but I was not quite so sure that the space allocated to the Virus Laboratory would be adequate. It might do for simple biology, but the esoteric type of research that Stanley and his associates conducted required much equipment and especially large items of equipment for both physical and chemical studies, so that space would be used up at a tremendous rate. I expressed my reservations, and indeed I was proved right because by the time the building was completed, it was evident that within another year or two additional space might well be required. In fact, some years later the entire building was devoted to virology, being renamed Stanley Hall after Stanley's death, and the department of biochemistry was sited in a new building on the western edge of the campus just off Oxford and Hearst Streets.

Hughes: Stanley Hall is right across from Donner Laboratory, and there was supposed to be a research collaboration between scientists at Stanley Hall and the medical physicists at Donner Lab.

Lennette: That's right.

Hughes: Was there any sort of understanding about your spheres of influence? Stanley, as I understand it, was much more interested in basic research on viruses, where you had a more applied epidemiological and diagnostic approach.

Lennette: No, there was no written agreement, not even as far as I know an understanding. Our fields were separate, and he was very much interested in basic and fundamental science, which we were not. We were not equipped to do that except in very superficial fashion. Our interest was mostly epidemiology, fieldwork, and clinical medicine, which explains some of our programs, for example the program on Q fever, the one on influenza vaccines, etc. But Stanley nevertheless was a very good friend, a supporter.

Well, first of all, I'd like to point out that Stanley and Malcolm Merrill were friends from way back, because they were colleagues at the Rockefeller Institute in Princeton, N.J. Merrill was working with [Carl] tenBroeck on encephalitis at that time, and Stanley on tobacco mosaic. So when Wendell came to Berkeley, they had a common basis for meeting occasionally, and Stanley found out what was going on down at our lab on University Avenue. Frequently the California State Legislature would raise the age-old questions that still are raised perennially

Lennette: for all the years that I've been here. First, they always talk about moving the laboratories to Sacramento, which has never happened. Number two, there is always talk, why should a state agency be doing research of any kind? That's the province of the university, which is a congregation of scholars. Well, Stanley recognized that there's a difference of approach to pragmatic medical and public health problems. You do have a continuum of medical, epidemiological, and other kinds of problems, on which you have to do some kind of research. Research is how you define it, actually. Anyway, he felt that there was no overlap in functions, or if there were, it was small. And before the legislature or its committees, he would always testify in behalf of the State Health Department.

Location, Construction, and Design of the Health Department Laboratories

Hughes: What was the reason for wanting it in Sacramento?

Lennette: Well, apparently it was an anomaly to have a health department which was not in the state capital. Why should it have its headquarters in San Francisco, which is where it was at that time, specifically in the Phelan Building on Market Street? The laboratories originally were in the Life Sciences Building of the University of California, Berkeley. I don't know whether it was by law or by regulation that they had to be housed there. Of course after the war, with the burgeoning expansion and explosion in microbiology, Life Sciences wasn't big enough to house our laboratories, nor all the other biological laboratories of the university, like physiology, zoology, or whatever. They were just being inundated with new information. So somebody had to move, and the easiest thing was to move out these intruders from the health department. So then we had to look for another home, another building.

In 1948-49 the health department's laboratories were small. We looked at a number of buildings here in Berkeley, but found conversion into laboratories would be virtually prohibitive from the standpoint of economics. It would be easier simply to start all over and go from scratch with a new building. The California State Department of Finance recognized that it had better go ahead and build a new home for the department. Here again, the department of health was shortchanged, just as was the university, by the legislature. This is now 1950, '51, when the federal government had matching funds for various projects. They contributed half, and the state contributed its share.

Lennette: The University of California at Berkeley decided to put up a school of public health. Money was available from the federal government from the budget which was put together by the dean, Charles Smith, as I recall, or maybe it was his predecessor. And we, too, were going to put up a laboratory, but we didn't have matching funds from the federal government, so the only money available was state money. The University of California School of Public Health finally went ahead and built the school with the funds which the federal government gave, which was only half of what was needed, so the final building was not adequate. What happened is a typical example of how a governmental agency behaves. You had something which from the beginning was inadequate, so you always had to keep adding on to it. That's how these excrescences appear on these buildings.

So far as the health department is concerned, this building in which you are now sitting was put up with the funds that were available in the state budget prior to World War II. So in 1950 or '51 we designed a building which cost whatever was appropriated in 1939 or '40, with no allowance for postwar inflation. We didn't get everything we needed, and there were a lot of things we had to sacrifice, plus contending with all of the stupidities foisted upon us by the architects in Sacramento. They had no idea of how to build a laboratory, and yet would not take the advice and suggestions of the people who were going to use the laboratories. Their attitude was, "What do these longhairs in Berkeley know. We're the engineers. We're the architects. We know what we're doing." So they put it up according to their ideas, and of course it was inadequate from the standpoint of function.

But with time we got more space. As I say, it wasn't adequate from the standpoint of space, but from the standpoint of security, I can't really fault the state, because they gave us the money we needed to build a laboratory in which we could contain these organisms in a fashion similar to that done at Camp Detrick, Maryland, our model.

Hughes: Were you the source of information on how to do that?

Lennette: Yes.

Hughes: And they listened to that part?

Lennette: They listened to that. Well, they did a lot of things that are kind of ridiculous. This building wing we're sitting in right now was built later as an add-on. We wanted the air intakes for the laboratories to be on the west side of the main building, on Shattuck Avenue. The air exhaust would be on the east end, on Oxford Street. So, much to our dismay, what did they do? The

Lennette: intake is right up against the outflow. And this is the kind of consideration they gave our planning. What we were planning on was to have clean air come in from the west side, that's the prevailing westerly wind, and have it come out on the east end of the building. Then by dilution, if there might be a contaminant, it would be dispersed. Of course there would be air incinerators in between. That's the way we set out to do it.

In the main building we were going to house somewhere between eight hundred and a thousand people, so we had to make some provision to protect these people. What you see as the entrance to the Virus Laboratory on the fourth floor is an air lock. The two doors are interlocked so that you can't open both simultaneously. You can go from one and, when that one closes, you can open the other. The airflow is such that there's a negative pressure in the laboratory, so if anybody did by accident open those air locks, the airflow would be from the administrative wing through the laboratories, not vice versa.

Now this calls for a balanced airflow; it calls for a knowledge of what's involved, maintaining these barriers and keeping the airflow constant. We had UV [ultraviolet] ducts, air intake, air exhaust. We had indicator lights to show that these were functioning. We had air incinerators set into the ceilings. Any air going out of the room wouldn't go out through the usual ducts; it would go out through the air incinerator. We had, in effect, a highly contained lab which the NIH some years later "re-invented" for its recombinant DNA work.

Hughes: Were these methods actually first developed at Camp Detrick?

Lennette: A lot of them were, yes.

Hughes: Was that a burden of the scientists who were called there for the war effort? I would think that before they began research, they had to get the building in proper shape.

Lennette: A lot of this was developed as they went along. There were some episodes of infection, but they weren't all that bad. In any case, anything that did happen on the post was restricted to the post. Nobody got infected at Camp Detrick and started an epidemic outside, in Frederick, Maryland. It was contained on the post. I mention this because all of the horrifying scenarios that have been written by molecular biologists and science fiction writers don't have to happen. Many of these proved methods and techniques of handling organisms and storing them, having access to them, were developed in Camp Detrick. These are still the criteria by which most people in pathogenic microbiology operate.

Lennette: Now remember, at the time this laboratory was built, there was no such thing as genetic engineering. They didn't know about DNA at that time. But we were fully aware of the hazards, because there had been laboratory infections elsewhere, and there had been some deaths. So when we designed this laboratory, we were quite conscious of the hazard that might be posed to the staff here. When the people in genetic engineering began to develop this field about ten or fifteen years ago, and became serious about production of new bacteria containing foreign genes, a stream of scenarios was written about the terrible things that would happen and how scientists would foul up the evolutionary process by producing strange new organisms, and unleash them on the world. All sorts of monsters would be created. Well, that was unfortunate. It led to questions being raised about how to protect the world because of these dire things that we're doing. This in turn led to establishment of a whole scheme of containment laboratories, graded in a scale of P1 through P4, i.e. from open bench top to absolutely rigid physical precautions.

Here on our fourth floor is a P3 laboratory. It had been operating for twenty years before the molecular biologists wrote this report. P3 labs are what a whole lot of genetic engineers are using today. As a matter of fact, in many labs they're down to P2 now because the awful scenarios did not eventuate. The P4 so-called is one kind of a laboratory that you will find at Camp Detrick, and which you will also find at the Center for Disease Control in Atlanta. The big problem is to keep an equilibrium that combines practicality with efficiency; don't make it so secure that the investigator can't get in because it's full of safety barriers and equipment.

Hughes: But none of the basic virologists had taken the time to examine the existing systems?

Lennette: Well, you have to remember that many of these people were trained in biochemistry, and like a chemist, they pour things from flask into tube, and if they spill a little, they sort of stamp it out with their foot. You can't do that with bacteria and viruses, or any living microorganism. You have to handle them circumspectly. The chemist stands up at his bench; the microbiologist works sitting down. It's a difference in the operation. The microbiologist is trained to handle everything aseptically, handle everything without contamination from the environment or pollution of it. His working procedure must be second nature. He doesn't have to stop to think, "Now I'm going to pull out the cork, the bottle stopper. Now I'm going to clean the tube, and now I'm going to pick up the needle and now clean this." He just does it routinely. It's a reflex. And this

Lennette: you develop only over time, with continual practice. As I said somewhere, I would just about give up on the present generation of biochemists and geneticists and start to train the new generation in the techniques of pathogenic microbiology. It's hard to teach on old dog new tricks.

Hughes: The legislature was sympathetic to all these special needs that you had for the new building?

Lennette: Yes. Well, you have to remember, we started all this under the administration of Governor Earl Warren. Earl Warren was very public health minded, very helpful, and always very supportive of the Department of Public Health. Now mind you, we were not a behemoth. We never were. People today blame and attribute to this health department all of the peccadillos, discontent, and scandals that really are caused by MediCal. We have nothing to do with MediCal, which is the huge part of the Department of Health Services--we're just a little bitty tuft on the end of the dog's tail. The rest of the dog is MediCal. But we get tarred with that same brush. At the time of Earl Warren we were a small and independent department, and our needs were fairly modest. The laboratories were small, and Governor Warren gave us, as far as labs are concerned, essentially what we needed.

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From the days of Governor Warren through the days of Governor Edmund G. (Pat) Brown, the department was an autonomous agency and had the full support of every administration until the advent of the Ronald Reagan regime.\* Governor Reagan's minions rather effectively emasculated the ability of the Department of Health to function and initiated its eventual decline and loss of leadership, then the self-centered regime of Governor Jerry Brown put the final touches to the demise of the department as not only a nationally recognized, but also internationally recognized, leader in public health. Thus, under Ronald Reagan a young physician, Earl Bryan, with little medical experience and no public health experience, was appointed director of the health and welfare agency, created by combining a number of departments, including Mental Health, MediCal, and the Department of Health. One of Bryan's first acts was to abolish the Board of

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\*Dr. Lennette wrote the following four paragraphs after the interviews had ended.

Lennette: Health, which provided guidance, support, and advice to the Department of Health, and take over these functions himself. The bureaucracy established by the Reaganites aimed at obtaining absolute political control over all state departments led to a ponderous machine with which it became virtually impossible to deal because of the numerous administrative levels involved. Thus, where in Governor Pat Brown's administration it required only two or three weeks to process a research grant proposal from the director's office through final approval by the Department of Finance, it now required nine months! The delay in large part was engendered by lay administrative officers completely ignorant of medicine, biology, and public health, who demanded that all grant applications be reduced to simple English which they could understand!

The department's national and international position of leadership was further eroded by the Jerry Brown administration which in turn appointed an attorney as secretary of the Department of Health and Welfare, again, an individual with no knowledge of medicine or public health but with a passion for social reform to which he devoted all of his time and efforts with little concern for the public health responsibilities.

The removal of all the health department's administrative functions from Berkeley to Sacramento, where they could be monitored and kept under the control of the department's political appointees, also adversely affected the operation of what was left behind, namely, the laboratories. Administrators in Sacramento, eighty miles from Berkeley, had and have little or no knowledge or appreciation of what role the laboratory plays in public health and medicine, and solve its problems by ignoring them.

This plus other adverse actions have brought the department down from a number one position of leadership and recognition to what I might say is, at best, a fifth rate operation. Laboratories, internationally recognized for their contributions to medicine and public health, are also rapidly losing ground through loss of talent, scientists leaving because of incredible bureaucratic red tape and also lack of support on the part of the Sacramento bureaucracy.

Hughes: Where did the department's fame come from?

Lennette: It came from things they were doing with child health, for example, infant mortality. A great deal of time and effort went into epidemiology and infectious disease. The laboratories were outstanding and models to emulate--not necessarily only the Virus Lab; the bacteriology labs, too, were outstanding.

The Virus Laboratory's Association with other Institutions

Hughes: How much cooperation did you have with the health department's Bureau of Communicable Disease or Vector Control? Was that just an incidental association?

Lennette: No. With the Bureau of Communicable Disease, at that time, the early fifties, we had very little interrelation, because that unit was mostly administrative. Thus, they used to file post cards, notifications that we've got a case of smallpox, or we've got a case of chicken pox, measles. They would put them in the right pigeon hole, and at the end of the week they'd count them all up: You got so many cases of this or the other. That's how diverse incidence was followed and studied, and epidemics or outbreaks studied statistically and in the field.

This changed with time to the point where Communicable Disease became a very important operation, and began to collaborate with us on the lab side. It goes back to the days when I brought James Chin, who's now the chief of the Bureau of Infectious Diseases, on the staff. He had been with the Hooper Foundation people and had been assigned to work in Kuala Lumpur in Malaysia. When that project folded, he was at loose ends. I got him interested in joining my staff and going down to Fort Ord to act as the epidemiologist and the leader of the project on influenza vaccine and respiratory disease. So during the few years he was at Fort Ord working with me on influenza, he learned a great deal about the role of the laboratory. We had several other people on the staff here in Berkeley who also passed through the laboratory to get a broader foundation of infectious diseases.

So what we developed, in effect, was a staff, both in the laboratory and in the Communicable Disease unit, which was cognizant of problems on the other side. We didn't have somebody from Infectious Disease coming in with a thousand specimens over a weekend wanting an answer on Monday morning. On the other hand, in the laboratories we didn't have people who couldn't understand what the problem was in collecting material from human subjects, and how difficult studies are when you are dealing with human beings and not experimental animals. In consequence, we had a very good rapport. It still exists.

Our liaison with Vector Control was different. It was much closer at that time because we were interested in the encephalitidies. These people were good at mosquito control, and very good in entomology and mammalogy. We were interested in mosquitoes as vectors for these encephalitidies--St. Louis and western equine primarily. Over the years Turlock virus and other viruses were

Lennette: discovered in this laboratory. California virus was discovered by people across the street at U.C. in the School of Public Health. The liaison with Vector Control still exists, and we continue to work with Dr. Bill Reeves and his associates in the U.C. School of Public Health.

We have never been isolated, nor have we wanted to be isolated, which is somewhat different from the university. I don't know about the social scientists, but in the biological sciences it seems that every investigator in an academic environment goes into his own cubbyhole his own monastic cell, and has no interaction with anybody around him on either side or up or down. He just goes his own way.

In contrast, we worked and collaborated with these various groups, and operated the same way across the bay with the San Francisco scientists in the Hooper Foundation and in the U.C. Medical School.

#### Karl Meyer

Hughes: I know Karl Meyer\* was a consultant to the State Department of Public Health virtually all of his career. Can you tell me about his interactions with you and the Department of Public Health?

Lennette: Of course he knew me when I was at Camp Detrick. As a matter of fact in 1946, before I went to Detrick, I had talked to him about whether I should go or not.

Hughes: Did he have firsthand experience?

Lennette: Yes, he was a consultant to Camp Detrick. He had been there during the war off and on as a consultant. He didn't actually work there; he was a consultant in various areas. I had luncheon with him several times and talked to him about the prospects, and he finally suggested that I go. He hated to see me go, but he thought that the career opportunity there would be better. He said, "Try out your wings; see how it goes." So it was partly on his recommendation that I went to Detrick.

He had done a great deal of work in bacteriology about which I don't know much because he was a giant in microbiology long before my time. I know what he did in botulism, for example, and in brucellosis. His laboratory also came up with the western equine encephalitis virus, showed it was present in man and equines, and was different from the one found in the East. He did some work on western encephalitis virus, but not a great deal, as his interests were elsewhere, in bacteriology.

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\*Karl F. Meyer, Medical Research and Public Health, an oral history interview conducted 1961-1962, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 1976.

Lennette: He also did much research on ornithosis, at that time called psittacosis, so much so that whenever there were outbreaks of any kind that our department would investigate epidemiologically, all the clinical specimens from patients or exposed individuals would go to his laboratory. We never got them.

##[tape interruption]

He was a source of information for us and a consultant, not only on the encephalitidies, but other problems as well. As I say, we collaborated with him since he was deeply interested in ornithosis research. We let him have all the ornithosis material. By law, if you want to get really technical about it, the department should have been testing it, because we were the legally responsible entity, not the Hooper Foundation. But he was already testing human material, and since he had the reputation, we just let him have the material. Of course after he died, and this work load was dumped onto our shoulders, we had quite a time! We had all that material we had not expected to test. It came from all over the state and also elsewhere.

Hughes: He, as I remember, tended to be more interested in nonhuman infections, was that not true?

Lennette: He was interested in the so-called zoonoses.

Hughes: He was the first to isolate western equine encephalitis virus--

Lennette: That's right.

Hughes: --in horses, and then somebody else came along, about ten years or so afterward, and isolated the virus in man. Was that [W. M.] Hammon?

Lennette: Yes. I'm not sure but what they also recovered it from a patient. I think it was Bernice Eddie, Meyer's associate, who isolated it from horse brain.

Hughes: [Ralph] Muckenfuss, according to my information...

Lennette: Muckenfuss discovered St. Louis encephalitis virus.

Hughes: He isolated it in 1933 from a human brain.

Lennette: Yes, he was chief of the laboratories at the St. Louis Department of Health.

Hughes: And then I have Howitt, who, I believe, was in California?

Lennette: Beatrice Howitt was here with K.F. Meyer. She, I think, got the virus out of a child.

Hughes: Yes, in 1938, according to this note. And then in 1941 William Hammon and [William] Reeves isolated western equine encephalitis virus from mosquitoes.

Lennette: That in itself is interesting. You mentioned Dr. Hammon. Until he arrived on the scene, there were no medical virologists out here except K. F. Meyer, Monroe Eaton, and myself; I think E. W. Schultz, at Stanford, had died a few years before. There was nobody else really in virology on the West Coast. We were sort of isolated out here. This was in the day of the railroad train, and it took a long time to get from New York to San Francisco. Because only three of us were here shows what West Coast virology was as a discipline. Hammon was trained both in the East and with K. F. Meyer, and learned a lot of virology there. We did it the same way, working with Hammon. This was the opening of virology in this area. And of course from that point on, you began to get more and more people out here after the war.

Hughes: Where was Hammon?

Lennette: I'm not sure where he came from in Africa--the French Congo, I believe. He was a medical missionary.

Hughes: Was he active in the department?

Lennette: He was at Hooper. Reeves was over here in the University of California School of Public Health, department of epidemiology. Hammon either moved over to the Hooper, or he was seconded to Hooper.

### Encephalitis Research

Hughes: Let's backtrack and pick up on the encephalitis. There was an epidemic of western equine encephalitis in California in 1952, but obviously there had been some work prior to that. For example, Reeves and Hammon found that the vector was the mosquito. What about finding that there was an endemic area for both viruses in the Central Valley? Wasn't that a rather striking discovery?

Lennette: Well, it took a lot of legwork, a lot of experimental work to establish that both viruses were present in the valley. A lot of work was done around Bakersfield, Kern County. As you mentioned, Meyer was interested in Zoonoses. This was an example of it. He and Hammon and Reeves studied all the animals there and the chickens and, of course, mosquitoes and

- Lennette: other arthropods. The upshot was that it was obviously a mosquito-borne disease. Different species of mosquitoes were involved. The chicken was thought to be the reservoir, for birds anyway.
- Hughes: Did Meyer and his group suspect this way back in the thirties when they began?
- Lennette: No, this was the work of Hammon and then Reeves, especially Reeves. And that's really where it stands. I don't think there's been much added to it.
- Hughes: You wrote several papers on the differential diagnosis of western equine encephalitis and St. Louis encephalitis.\* Was that a technical point since the symptoms were the same and the treatment was the same?
- Lennette: Yes, it was mostly supportive. The distinction was made in the laboratory so that you had more accurate statistics on what had occurred. Let me give you a very good example of that, one which is really outstanding, and that is poliomyelitis.

Poliomyelitis is an example of how diseases can be misassigned etiologically. Whenever you saw a year that had a lot of paralytic disease, a lot of these minor illnesses were labelled nonparalytic poliomyelitis. In other years these were pretty much ignored, because there was no indicator involved. In other words, there were a lot of cases being paralyzed, so you knew you had poliomyelitis, and a lot of the minor illnesses without an attending paralysis were called nonparalytic polio.

Then when Nathalie Schmidt and I designed a diagnostic complement fixation test, and other people designed the so-called metabolic inhibition test, we had methods for specifically diagnosing poliomyelitis. We had tests for western equine, St. Louis encephalitis; we had tests for lymphocytic choriomeningitis. Now, when we began to make specific laboratory diagnoses of poliomyelitis, all this huge incidence curve that used to shoot up to the top of the chart in the summer and then fall down in the fall, called nonparalytic poliomyelitis, essentially disappeared, because it was a catchall for a lot of other diseases which we

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\*Edwin H. Lennette and W. Allen Longshore. "Western equine and St. Louis encephalitis in man, California, 1945-1950." Calif. Med. 75 (1951):189-195.

Edwin H. Lennette, Marjorie C. Nyberg, Dolores M. Barghausen, Roland Chin, Francis Y. Fujimoto, and Margaret K. Itatane. "The 1952 outbreak of encephalitis in California. Laboratory methods for etiologica diagnosis." Calif. Med. 79 (1953):78-83.

Lennette: could not diagnose. We didn't have the facilities; we didn't have the techniques for diagnosing the diseases in this potpourri of illnesses.

The same thing when Q fever came along. It used to be called brucellosis. The incidence of brucellosis was horrendous. But once we could make the diagnosis in the laboratory, specifically say this is a case of Q fever, the incidence of brucellosis fell dramatically.

Now, today, you don't hear much about Q fever. I haven't seen the data, but I would suspect that the curve for brucellosis or for something else similar has gone up.

Hughes: Was that perhaps true of encephalitis, too?

Lennette: Probably. There are a lot of silent infections, so-called, minor infections.

Hughes: In a paper published in 1951,\* you speculated that there must be a lot of as yet unidentified encephalitis viruses. You knew about the western and you knew about the St. Louis. Why did you make that speculation?

Lennette: Because they were isolating these viruses from mosquitoes. Man was exposed to these mosquitoes which could very well be vectors of these viruses. And California virus was one of them. That was what Reeves was doing in the U.C. School of Public Health. This was some years later. They recovered the California virus in mosquitoes and subsequently found human cases of it.

We discovered Turlock virus in mosquitoes, but we couldn't identify it, and finally typed it out as a brand-new virus. We found human cases of it and we went back and tested it. As a matter of fact, for some years all the specimens of blood that were collected across the street at the U.C. School of Public Health were sent over for us to check for Turlock virus. We didn't find a huge number, but we found some. And Dr. Reeves and his group were trying to sort out how many viruses were involved in producing all this morbidity.

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\*Edwin H. Lennette and W. Allen Longshore. "Western equine and St. Louis encephalitis in man, California, 1945-1950." Calif. Med. 75 (1951):189-195.

Hughes: Can you give me a feeling of how the epidemiological studies of encephalitis were conducted?

Lennette: Well, when there were obvious cases of encephalitis hospitalized, the health officer was apprised, of course, because it was demanded by law that you notify the health officer. And that way it came to our attention. It would go through the health officer directly or casually through a physician who knew somebody here in the department. So we knew when cases of frank clinical encephalitis occurred. Then we would arrange to get specimens of blood. Obviously the virus was found in the brain, and we couldn't go into the brain so we had to detect it by serologic tests. So these specimens were sent to the laboratory, and in the early days somebody in the epidemiology group, either from the local health department or from here, would interview these patients, get a clinical history and find out where they'd been travelling, how much exposure they had to insects. Typical epidemiological shoe leather approach.

Hughes: The Bureau of Communicable Disease handled that?

Lennette: Yes. Of course, our resources were too slim to do all of this, but they had help from the local county health departments.

Hughes: And were the local departments very cooperative?

Lennette: Yes.

#### Training Physicians in Virological Techniques

Hughes: In paper after paper you hammered home the point that the accuracy of, the methodology of, specimen collection makes all the difference in the world. How in general did physicians in the field respond to those directives?

Lennette: Well, it all depends on how you phrase your question. Either you get a little response from me or you get a diatribe.

Hughes: I'll take a diatribe. [laughter]

Lennette: When I first came out here, a great deal younger than I am now, I was trying to educate the whole medical profession to becoming virologists. [laughs] I would go out to the local hospitals here within reach and meet with the staff and occasionally give a lecture before the county medical society. Then I soon found out that I was just spinning my wheels, because I would talk to the house staff, let us say, at some hospital and get them all imbued with enthusiasm of finding these cases that they were missing, of

Lennette: how to get the specimen. Then I had to do the whole thing over next year for a whole new house staff. It's a continuous process.

I then began to focus on the medical schools. If we could just educate medical students about infectious disease the way we were trained. As a matter of fact, indirectly this was brought up yesterday by several physicians. I attended a lecture at Herrick Hospital, one of a series of four lectures, a mini-series, on infectious disease. It was pointed out that those hospital-acquired infections, so-called nosocomical infections, are quite a problem. Somebody pointed out, "Well, they don't do what they used to. Physicians go directly from patient to patient, no sterile precautions. At least you used to have to wash your hands. They don't do that any more." That's one indicator of what's transpired.

The coming of molecular biology and the emphasis on molecular virology, which of course has given us some tremendous advances technologically, unfortunately has diffused the teaching of medical bacteriology, parasitology, and virology to the point where the medical student is taught by people who are primarily biochemists, geneticists, an occasional M.D. There's nobody more radical and fanatical than an M.D. who's gotten into the basic sciences, specifically molecular biology. It's like a religion. They don't teach the students the medical aspects, so these future physicians are shortchanged. Thus, a student comes out of medical school; he knows what DNA is; he knows how many turns there are in the spiral; he knows how many angstrom units there are between each turn, that it goes from left to right, all this sort of information, which he will rarely use. He should have some exposure to that, sure. Intellectually, he ought to know what's going on in the world. But insofar as he is concerned professionally, this is of very little use to him.

More cogently, what he needs: Here is a patient with an infectious disease. Before he sees that patient, he should put on a gown; he should probably wear gloves; at least he should wash his hands. Before he goes, he should leave behind his gown, his booties and cap, the way they used to do it in the old days. When he goes to the next patient, he repeats the whole thing. This is not done at the moment. I think in large part it was done originally because doctors were afraid to get tuberculosis from patients, because tuberculosis amongst medical students and interns was high.

Lennette: Well, this methodology has disappeared with time. They no longer house patients in an infectious disease hospital. They put them right on the same floor with other patients in a general hospital. Furthermore, they used to keep children out of these institutions. Now these kids run up and down the hallways and knock you down. They're just transmitting microorganisms from patients, and passing them on elsewhere.

This is where part of the nosocomial problem lies. Not all of it, but part of it. We just don't train our doctors, and our nurses for that matter, in all of the techniques we know that in the past were useful in containing infections. We might not stop them all, but we could certainly cut back.

Hughes: Did you try to get this point over to the powers that be in the medical schools?

Lennette: No, I didn't have enough clout. I was just a young fellow in medical virology. There weren't many medical virologists. It got so that when I complained to my colleagues, I got the stock answer, "But doctor, you don't understand academic medicine." Well, I don't understand academic medicine. I always thought that the idea of academic medicine was primarily to train practitioners, not researchers. If somebody wants to do research in medicine, he'll do his internship and then go on for two or three years, and then go to the Rockefeller Institute, this kind of thing, get some research training and then go out and do research. But these schools take the attitude--this isn't entirely fair--that every student that comes in has got to be a researcher, an investigator of the highest merit. Well, people are born with that talent or they aren't. It's the responsibility of medical schools to train practitioners. I could never see what's wrong with that.

So I fought my colleagues in microbiology because microbiology is a science per se. In other words, in microbiology you have an organism and you study that organism to see what it does. How does it react with man? What does it do to him? How is he going to defend himself? That's medical microbiology. Parasitology is even worse off. Now it's undergoing rejuvenation, a revival, because the molecular biologists have gotten their oar into the parasitology field now; some really nice work coming out now. But what I'm saying, this is not the end-all, be-all of medicine. It's a valuable contribution, but this isn't what you're educating your physicians for.

Hughes: Were you troubled all the way along with specimens that were submitted for diagnosis that were not properly collected?

Lennette: We still have the same problem. Physicians and technologists still don't know how to take clinical specimens, although this has gradually ameliorated. As antibiotics came along--at first it was penicillin--there was the unfortunate attitude amongst physicians, and especially health officers, that there was no longer a problem with infectious disease; it was all conquered. Just go on to other matters, like the social aspects, and don't worry about infectious disease.

Well, all that antibiotics do really, when you get right down to the nitty gritty and look at the data, is prevent deaths. They have not affected the morbidity one iota. We still have the same number of cases as we had before. We just have fewer deaths. So now they've realized that they still have an infectious disease problem.

Finally, we are now finding people who are truly specializing in infectious diseases. I haven't seen one of these specialists for years. Nobody in his right mind went into infectious disease, especially viral infectious disease, as a specialty. Now they have one on every hospital staff, not necessarily because it's a great problem of infectious disease so much as that there are so many antibiotics, especially in the penicillin family, that you need one person just to follow all the literature and decide which ones to use! If you get a problem, you call in the infectious disease physician, because he knows which antibiotics to use. That's how far it's gone.

But in any case, there is a reemphasis, a real renewal of interest, in infectious disease. So I think that these people now have to know how to collect clinical specimens. Virology is coming of age, and they're going to have to know about it.

It's important to know your limitations. If the physician doesn't know--and I don't fault him on this; he's a clinician; he's primarily at the bedside--and he suspects something, he ought to have a pathologist that he can consult, and the technicians ought to know how to collect specimens.

Hughes: And they don't, in general?

Lennette: They know how to take them, but they don't know all of the ramifications, how many days apart to collect specimens in acute and convalescing and recovery patients.

##[telephone interruption]

Lennette: When I was doing infectious disease work at Highland Hospital, Alameda County, I was on the consulting staff, and I would go into the clinic, and there would be a lot of patients sitting out there, some with, let's say, symptoms reminiscent of meningitis. The first thing that would happen, some house officer or nurse would give them a good dose of penicillin. By the time that patient was seen and the requisite spinal tap was done, maybe an hour or two hours had gone by. By that time the penicillin was working, so that if you examined that spinal fluid, if it were a viral disease, it wouldn't make too much difference, but if it were a bacterial disease you couldn't tell if it were pneumococcus or meningococcus or Hemophilus influenzae. So you were stymied as to what kind of treatment to give. These are the sorts of possibilities one has to keep in mind. These were the early days I'm talking about, the 1950s. People are a lot more cognizant of these things now. But that's all part of practicing medicine.

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#### Current Work on Three Books

Hughes: Please comment on this book on laboratory diagnosis that you are writing.

Lennette: At the moment I am actually working on three books.\* The first, which represents a tedious and time-consuming task if one is to be conscientious, is a revision of those portions of Stedman's Medical Dictionary dealing with virology and immunology.

The second is a short book, relatively speaking, concerned with the laboratory diagnosis of viral diseases. The traditional book dealing with infectious diseases is a rather large and comprehensive volume, the chapters generally beginning with a brief history of the disease; for example, poliomyelitis, and how evidence of its presence in the Egyptian population was revealed by typical deformities found in mummies dating back to 4000 to 5000 B.C.; and in thorough descriptions of the clinical aspects, epidemiology, immunology, pathogenesis, etc., and including a general discussion of laboratory diagnosis. Unless one is a

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\*Dr. Lennette wrote the following section on his books after the interviews were completed.

Lennette: medical historian or anthropologist, one has little use for a presentation that requires so much pagination, and pages are what you pay for in a book. The book I am currently editing, Laboratory Diagnosis of Viral Infections,\* will have a brief presentation on clinical features, basic background information on epidemiology, pathogenesis, and specific treatment, but only to provide the structural background for a thorough discussion and presentation of laboratory approaches to diagnosis. For example, there will be a description of the causal agent involved in the specific disease, perhaps an electron micrograph to illustrate what it looks like, etc., all pointed towards information forming the basis for laboratory diagnosis. This book is to be produced under the aegis of a commercial publisher, which means that royalties are involved. But since scientific books generally have a limited audience, a royalty income is miniscule, but young and naive authors have visions of a Mercedes-Benz in the royalty picture. Factually, my last royalty check on a book produced a few years back was forty-six cents! I did not cash it and the publisher wrote me, "Why don't you cash your royalty check." I said it would cost them a dollar to cash that check for forty-six cents but they insisted I do so to meet legal requirements and also to facilitate their bookkeeping!

The next book in which I am involved will be the fourth edition of the Manual of Clinical Microbiology of which I will again be the editor-in-chief.\*\* Virology will be only one section of this book which will also deal with the laboratory diagnosis of bacterial myocarditic and parasitic diseases. It is to be published under the sponsorship of the American Society for Microbiology and is purely a labor of love, as no royalties are involved.

Also under consideration is my bringing out the sixth edition of Diagnostic Procedures for Viral and Rickettsial Infections, which is really an in depth treatment, virtually a treatise, on laboratory diagnosis of this group of diseases. This book, in fact, is the bible of the medical virologist concerned with laboratory diagnosis, since it is a learned presentation by experts on given diseases and concerned with factual detail of laboratory methods and techniques.

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\*New York: Marcel Dekker, Inc., 1985.

\*\*Washington, D.C.: American Society for Microbiology, 4th edition, 1985.

Hughes: Why did you and Nathalie Schmidt take over as editors of Diagnostic Procedures?

Lennette: It was either Francis or Smadel who asked me to take over. I think it was Dr. Francis. The diagnostic field was getting pretty large; a lot of new viruses had been found, and he didn't feel that he had the time to keep up with all of these developments. After all, he was chairman of the department of epidemiology, running a big respiratory disease research program, and had a lot of other irons in the fire. He and Joe Smadel, who was one of the early coeditors, felt that this laboratory, which was doing so much diagnostic work, would be a natural. And of course since Schmidt was my colleague, I invited her participation, and the two of us decided to do it.

Well, our names have been associated with that book ever since, because that book, as I may have mentioned, became the bible of every diagnostic laboratory worldwide. It's hard to find a laboratory such as ours that doesn't have a copy of that book. It's very popular.

Hughes: Will you continue to edit it?

Lennette: Yes, I will. I don't know about Nathalie. She may feel that she wants to go on to other fields. If she gives up and I give up, that would be the passing of an era. That book would never have quite the flavor that it has now, because it was so closely intertwined with the California Department of Health, so that everybody expects that book to come out of this department.

### Q Fever

Hughes: Shall we go back to Q fever?

Lennette: Yes.

Hughes: There had been outbreaks in Australia. The first one reported was in 1935, and very soon thereafter E. H. Derrick named it Q fever, meaning Q for query. During World War II and thereafter there were outbreaks in Europe. In 1947 Frank Young discovered Q fever in California. Who was Frank Young?

Lennette: He was a local practitioner in southern California in Artesia.

Lennette: Derrick was the director of the Queensland Institute for Medical Research. He was interested in an outbreak of disease in a local abattoir. It was from this small outbreak of infectious disease that they recovered an organism which they thought initially was a rickettsia. They described the organism and were later proved correct. It was subsequently named Coxiella burneti by Derrick; the species for Burnet, who was an Australian microbiologist and immunologist and director of the Walter and Eliza Hall Institute for Medical Research in Melbourne; and the genus for Herald Cox.

They now had the organism causally responsible for this outbreak, which Derrick described clinically. He also described in a series of papers what he thought the spectrum of disease was like, what systems it involved, how it was contracted, and what the vector was. He thought the vector was the tick itself. Everybody thought this was a strange, Australian disease. As a matter of fact, some people gave it the designation Queensland fever. But Derrick himself told me, no, that isn't so, it's Q for query, as you've just said. He was here in Berkeley in 1950 or 1951 to visit our field operations. Subsequently Derrick and I got to be pretty good corresponding friends.

Frank Young described the disease he was seeing in Artesia, which to him was sort of a medical curiosity. I'm not quite sure about the background of all the events, but there were some cases of Q fever described in the Journal of the American Medical Association. Young was reading the journal when it struck him that he'd been seeing a few patients like those described and with what he diagnosed as atypical pneumonia. He thought that maybe his patients ought to have some tests done, so he drew some bloods and shipped them off to NIH or CDC [Center for Disease Control]. And the answers came back, yes, they were positive for Q fever. Shortly thereafter Charlie Shepherd of CDC came to California, to the Downey and Artesia area, and tested suspected recovered patients for Q fever, and found positives. This was in early or mid '47.

Robert J. Huebner was sent out by the U.S. Public Health Service. He came from the National Institute of Allergy and Infectious Disease in Bethesda, Maryland. This is about the time I arrived in California, all fired up to work on Q fever, too. So we divided the turf between us. Bob Huebner took southern California, and I took northern California. We each assembled a team.

The team that Huebner had when he came out here gave him the support that he needed--Dorothy Beck, an epidemiologist, Hartwell Welch, an entomologist, and a veterinarian. I think it was one of our veterinarians, Ben Dean, but later one of his own, John Winn and also Lauri Luoto. He also had a couple of laboratory people.

Lennette: Huebner was an indefatigable worker; he just worked continually. And very brilliant, very good at getting people to work together. He would get the whole team late at night--everybody was exhausted and tired--and he would issue orders for the next day. "This is what we're going to do, people. I want you all here at seven o'clock tomorrow morning. We're all getting out in the field. We're going to do this, that, and the other thing." Everybody arrives at seven o'clock; everything's changed. His staff had to do something else! And that's the way he operated. But he did contribute an awful lot.

He antagonized a lot of people because of the way he worked down there. One dairy reputedly threatened to give him both barrels if he didn't stay off their premises.

Hughes: Was he shutting dairies down?

Lennette: Well, he was just about shutting them down because he was showing where the rickettsiae were coming from, the milk, and the dairies certainly didn't want that. Then he had a running battle with others, because southern California, especially the Los Angeles area, was great on what they call certified milk, which to us people in microbiology and in public health is nothing more nor less than just a high grade raw milk. No matter how you cut it, it's raw. Nothing is done physically to it to kill bacteria or other microorganisms. He was sort of ruining the certified milk business, which was a huge, multimillion dollar operation.

With his team there, he worked out much of the epidemiology of Q fever: that the organism is present in ticks, that these dessicated ticks, which were ground up into the soil... Well, it was also present in cows' milk; it was also present in these ticks; it was also present in the excreta. The reason the disease was so heavily endemic in that area is that the dairy industry is a highly superficial affair. There are no cattle raised in Los Angeles. They all come from the valley up around Tarzana. Young animals are transported into these dairy herds. They come in; they are Q fever negative. After they were there a few months, the whole herd would be positive. All the newcomers were infected. These were the source of the rickettsiae in the milk. You wondered sometimes the milk was fluid, it was so heavily infected with rickettsiae.

Huebner worked out a great deal of the epidemiology--how the disease was transmitted by tick bite; how it's transmitted by air. The farther you are from the infected aerosol source, the fewer cases you had. Down along Imperial Boulevard they had one of the world's largest accumulations of cow manure, just mounds of it. Any time the wind would blow hard, it would create wind devils. This would take the rickettsiae right downwind. So a lot of cases came from that, and Huebner worked all of this out epidemiologically.

Hughes: Was he the one that was responsible for establishing the field lab at Hondo?

Lennette: Yes.

Hughes: Were you actually there?

Lennette: Well, I visited the lab occasionally. I didn't work there.

He had done some earlier work on a rickettsia disease called rickettsialpox up in New York City, so he was familiar with rickettsial agents. I was not.

Hughes: So that was why he was sent out?

Lennette: Yes. He had done a beautiful job showing how rickettsialpox was transmitted from the mice in the affected apartment houses in the Bronx; all the mice running around and living in the furnaces in the basement of the apartments. That was just a wonderful place for them to hide and breed. They were passing the disease throughout the apartment house. He had done a fine job, and, as a matter of fact, it was written up in several articles in The New Yorker.

Now he and I didn't get off to too good a start here in California. I considered myself an established investigator, and here's this young fellow coming up here trying to tell me how to do these serologic tests. That didn't sit too well. As far as I was concerned, he was the newest boy on the block, and he had to prove himself. But afterwards we got to understand each other and became very good friends. As a matter of fact, he's retiring on the eighteenth of September [1982]. He did a splendid job on everything he undertook and has had a brilliant career. He was elected into the National Academy of Science and showed the role of oncogenes, which he and George Todaro discovered, in the causation of cancer.

I was working up here out of Berkeley, and had my team quartered in the Virus Lab at Acton Street. Hartwell Welch came up here from Los Angeles to join us.

Hughes: Hartwell Welch was a CDC person?

Lennette: No, he was with the Bureau of Vector Control. At that time our laboratory was on Acton Street, that little bilious-green stucco building. We had a team that was comprised of departmental people. The director assigned Dr. William Clark as our epidemiologist. Hartwell Welch came from Vector Control, seconded to my operation. In other words, Vector Control paid his salary, but they didn't tell him what to do or anything else. All his orders came from me.

Lennette: The veterinary group seconded a veterinarian, Francis Abinanti, and CDC sent me a veterinarian, John Winn, and a third veterinarian, Monroe Holmes, of our department, worked with us briefly. So I had two veterinarians, an entomologist, an epidemiologist, a nurse, Mary Romer, and of course my own staff in the laboratory. We did all our own serological tests and inoculated field and human clinical materials into lab animals, guinea pigs and hamsters.

Then we got to a point of discrepancy between the southern California group and our own. Naturally we started out studying the cows in northern California. We thought, from the Los Angeles studies, these are the beasts that are causing the problem; let's get with it! But our serologic tests essentially were negative. Only a very small proportion of cattle, less than two percent, were positive. So we said, this can't be. Of course Huebner's attitude was, "You guys don't know how to do the test. You're missing infected animals."

Well, the truth was somewhere in between.\* We just did not have the counterpart kind of dairy husbandry in northern California that they did in the Los Angeles area. The dairy cattle in northern and central California are part of a herd all year round. They are born into the herd and they reproduce as part of that same herd. This is the natural course of events, quite different from the artificiality of the animal husbandry practice in southern California. There an isolated dairy would import non-infected animals, susceptible animals from the southern part of the Central Valley, as I mentioned, and the infection would thus be maintained in that herd. The dairy, originally at the periphery of a town, would eventually find itself encircled by housing developments, and eventually would become surrounded by a considerable human population. And this of course is where the problem lay because everybody in the neighborhood was exposed to infection from the contaminated dairy.

Up here the infection cycle was not in cattle; it was in the sheep and in goats.

Hughes: Now why was that?

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\*Dr. Lennette wrote the following section on Q fever after the interviews were completed.

Lennette: In part it was due to differences in the animal husbandry practices. We found goats to be infected and the infection to be maintained within the herd, which generally was a closed herd with relatively few introductions of outside noninfected animals. A survey of dairy goats in the Greenfield area of Monterey County showed the infection prevalence rate to be very high, a rather disturbing finding since many mothers supplemented the dietary regimen of young infants and young children with goat milk.

The goat population is relatively rather small, and it appeared to us that a more important element in the maintenance of the infection cycle in nature was in sheep. Sheep in northern California are not raised primarily as a source of meat, but for wool, and the wool industry is a very important one to the economy of this state. Sheep husbandry practices are such that most of the lambing occurs during the winter months, namely, late January and February into early March. Infected placentas, which contain huge number of rickettsiae, are dropped and then ground into the soil by the hooves of the animals. Eventually the soil dries out during the dry season and, as the animals tramp over it, it gives rise to aerosols which infect other animals, including man. Q fever is thus pretty much an occupational disease primarily affecting males involved in the sheep industry and of working age. The seasonal incidence reflects such activities as lambing or shearing, and other individuals, including women, are secondarily infected through exposure to infected fomites.

Our studies revealed such instances as where a woman developed Q fever which was traced to contaminated clothing worn by the husband. The husband, returning from his daily chores removes his overalls or coveralls, hangs them up on an outer porch, and the woman of the household, in taking down the clothes preparatory to washing them, is exposed to dust which rises from the garments.

Hughes: She inhales it.

Lennette: Sure, she is infected by inhalation of rickettsia-containing dust. We had a number of such cases. All of these were anomalous and were hard to explain until we discovered that the rickettsiae were present in the dust, and the soil was infected with rickettsiae derived from placentas and from excreta. We worked out the epidemiology of the disease and also did a great deal of clinical study with patients seen at the Woodland Clinic and also at Red Bluff. Much of this was done in connection with studying the therapeutic efficacy of aureomycin, the first wide-spectrum antibiotic, first developed against bacteria but also believed to be of use in rickettsial infections.

Lennette: A nurse, Mary Romer, assigned to us from CDC, helped in much of the epidemiology by following patients for us, and also checking on those who had received aureomycin therapy, which was a separate chapter in our studies.

Hughes: You wrote a paper in 1948 on aureomycin treatment.\* Wasn't aureomycin barely on the market at that time?

Lennette: I was just getting to that. Just the other day we were talking about Q fever at a staff meeting here in the department. And they brought up the matter of chronic Q fever and especially the occurrence of endocarditis, as if this were a new discovery. I said, "Doesn't anybody ever read the literature? All of this was known thirty years ago."

Now Bob Huebner had described such cases, and there was one patient that Bob and I were very closely following for several years, a woman by the name of Opal Franklin. Opal Franklin had a clinically-diagnosed Q fever endocarditis. She had had a real hard attack of Q fever. When she died some years later, an autopsy was done, but Huebner was out of the country, so he never did get that material to really prove that that's what she had. Subsequently the British and others isolated the rickettsiae from the heart valves of patients who had endocarditis.

If you will go back to about 1948, you will see that Gordon Meiklejohn and I wrote an article introducing and pioneering the use of aureomycin for the treatment of Q fever. We didn't know what we were doing, since we had no data on dosage or the route of administration, but we were using it. [laughter] We also described a whole series of about eighty patients in which we pointed out that a large proportion had hepatitis, liver involvement. Furthermore, this wasn't original with us. Derrick had already mentioned this in some of his papers. So, where he had a few cases, we had more, and we just gilded the lily. Nobody had looked at the lily, let alone the gilt.

So to get back to aureomycin. Lederle had just produced this new antibiotic, which they called aureomycin because it had a golden color. There was a picture in the San Francisco Chronicle of Dr. Herald R. Cox standing in the doorway of this aircraft, getting off the airplane. He had a little box containing ten thousand dollars worth of aureomycin, which was going to be used

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\*E. H. Lennette, G. Meiklejohn, and H. M. Thelen. "Treatment of Q fever in man with aureomycin." Ann. N.Y. Acad. Sci. 51 (1948):331-342.

Lennette: by the California State Department of Health. Now ten thousand dollars today doesn't sound like very much, but thirty years ago ten thousand dollars was a lot of money. It was a big investment.

So we had aureomycin. Now they had known from laboratory work that it was quite effective with bacteria, but nobody really knew what the dosage was or how to give it, by mouth, by injection, intravenously or intramuscularly. Gordon and I had the aureomycin here. He was assistant professor of medicine at UCSF at that time, very good clinician. We decided to give it intramuscularly. We didn't know what dose to use. Well, this stuff was so acid that the minute we got the needle in, these patients practically jumped off the bed and hit the ceiling, it was so terribly painful. So we learned we had to dilute it out and neutralize it to get the pH down. That was the first thing. We didn't know what dose to give, so we just empirically decided the dosage.

###[telephone interruption]

Hughes: Did you have any particular reason for choosing the intramuscular route?

Lennette: Well, we felt that, like many of these other drugs that are still crude, it might be nauseating and the patient wouldn't hold it down. This way, we'd know how much we gave. So we had a small series of cases which all did very well. However, we had one twelve year old child to whom we didn't give aureomycin, which was fortunate, because a few days later he developed acute jaundice. Had we given him the aureomycin, the aureomycin would have been blamed. A good drug would have been tarnished right from the beginning.

On the other hand, we had one man who was at Kaiser Hospital here at Oakland. We gave him aureomycin every day for thirty days. We were worn out going down to the hospital every day, and he wasn't making any progress. So we finally gave up and stopped injecting him and a few days later he recovered.

Well, this was an early demonstration of suppressing the immune mechanism by overtreatment. There were many instances subsequently, with other diseases, but this was one of the very first. We didn't realize we were overtreating him. Once we stopped giving him all that aureomycin, he developed his own antibodies and recovered. So this was our experience with aureomycin.

Hughes: Did it become a recognized treatment for Q fever?

Lennette: Yes. Still is pretty much. There are other drugs available now. You can combine them.

Hughes: What about the vaccine?

Lennette: We made up the vaccine on our own. It was pretty crude stuff; it wasn't a very good vaccine. But then we learned that the rickettsiae have two phases, phase one and phase two. And we learned something about the structure of rickettsiae, something about the antigens. So the vaccines today are an entirely new approach.

Hughes: What was the financial backing for the Q fever studies?

Lennette: That was one of the first grants we had in the department which came from NIH. This was '48.

Hughes: So the state wasn't putting in any money directly into that project?

Lennette: No, we had those grants from NIH for a number of years, and finally they were terminated because the study sections asked why should they be supporting studies on this exotic disease which occurred nowhere in this country except California? Well, of course, since then it's been found all over the United States. I don't know whether it spread or whether it's always been there; I suppose the former. But it has come up to the fore again as an important disease.

Hughes: After Q fever was found to be endemic in California, a state advisory council was founded. What was the role of that council?

Lennette: The focus of that advisory group was primarily, what do we do about the dairies and the dairy farmers? The cows were heavily infected with rickettsiae, and we were getting cases of Q fever in people who were drinkers of raw milk, and in dairy workers who were surrounded by a contaminated atmosphere. We mentioned how artificial dairy husbandry is down there in the Los Angeles area. You've got these enclosures where the cattle are kept, and of course, as manure accumulates, the cattle get higher and higher up off the ground, to the point they can probably step over the fence. At that time, the dairy people bring in bulldozers and clean out the premises, and that's when you begin to get a few cases of Q fever, either amongst the employees or amongst the neighbors.

Hughes: So it was a matter of cleaning the barnyards out? And educating?

Lennette: Yes, I think that board was mostly set up to advise and to take care of the milk problem.

Hughes: Is there anything else you'd like to say about Q fever?

Lennette: No, except that it had occurred in a number of places before much cognizance was taken of it. It occurred amongst our own troops here in this country when they came back from Europe. There was a big episode down at Fort Patrick Henry, Virginia.

Hughes: Where would they have been exposed there?

Lennette: They were apparently exposed in Italy.

Hughes: Farmyards?

Lennette: Yes. Well, you know how the peasants live. They keep all the animals down in the lower part under the house, and their living quarters are up above the animals. That's how a lot of cases of Q fever occurred in our troops, because they were bivouacked with these people. The troops were moving out, and all these cases of atypical pneumonia in the returning troops were acquired from livestock. But nobody knew what the disease was until disembarkation in Fort Patrick Henry. The German troops in Greece suffered a huge outbreak which was subsequently shown to be Q fever. It really knocked them over.

Hughes: And still people were thinking that Q fever per se was confined to Australia.

Lennette: Yes.

Well, before we leave Q fever, there might be one other thing here. At U.C. San Francisco a few years back, several people contracted clinical Q fever, and it was shown that it was due to sheep. K.F. Meyer and Julius Schachter published a paper describing the episode and suggesting a remedy. Nothing much was done until they had a second episode just a few years or so ago.

They had several cases of illness reported from different parts of the Bay Area, mostly from across the bay in San Francisco, out in Marin. These were cases diagnosed as Q fever in the San Francisco lab or in our lab. And somebody going over the data with the health officers noticed this accumulation of cases, that they all seemed to come from UCSF in one way or another. So they looked into it, sure enough, that's where they were exposed. Well, one of them was an elevator repairman. He had just retired and was working there as a supervisor. He contracted Q fever and died. So the whole Q thing opened up.

Well, anyway, it was found to be in sheep right next to the hospital. The way the thing was handled didn't make sense, taking infected animals past laboratories where people were working or, for that matter, using common elevators and exposing them, plus all the airflow outside from the incinerators. There was quite a report on that. Well, they finally spent, I think, five hundred thousand dollars.

Hepatitis Research

##[Interview 4: November 4, 1982]

Lennette: My assignment, as I said, was to work on the experimental side of hepatitis, so we had a whole, big animal room in the back of 1392 University Avenue, with newborn hamsters, newborn cotton rats, newborn mice, and occasionally a ferret, all of which had been inoculated with material from patients with known hepatitis. We kept these animals around for days and weeks, and even for some months, and nothing much seemed to have happened to them. It didn't take very long to fill that animal room. So we had a huge animal room with some turnover, but in essence it all came to nothing. We never found any animals that became overtly ill attributable to the inoculum, and this was a rather sterile two-year period from that standpoint.

Interestingly enough, all of the data that we accumulated were eventually sent to Dr. John Paul at Yale, who was also very much interested in the hepatitis problem. He received data from a number of laboratories similar to what we sent, collated the information, and published a report, acknowledging where the materials had come from and the experience of each of the investigators. This was, that despite all the time and effort and money that had been expended, nothing was uncovered that was of any value. So that was a big drain on time and effort.

Training Physicians in Virological Techniques (continued)

Hughes: I think we already talked about the fact that it was a continuing problem to get specimens collected properly.

Lennette: It is a continuing problem. It's one about which I get very vociferous at the inadequacy of medical education today. Although I'm a physician, I was brought up as a scientist, and so it always hurts me when I see some of these things being done without full knowledge of what's involved, for example, statistics and the need for information. So a laboratory, if it's any good, needs a good clinical history just as much as a pathologist needs one, or an internist needs one if he's in for a consultation. You have to have something to put your teeth into. To send a specimen and ask just that it be tested for something is all right if you know what you're about, but that is open to debate now with many of the younger people.

Lennette: Collection was cumbersome, and we tried to explain what happened in the laboratory. We explained that many of these viruses would not survive at room temperature. Some you had to freeze down and you could keep them in the deep freeze. Others wouldn't stand deep freezing; you had to keep them on dry ice at seventy to seventy-five degrees below zero. We tried to be as scientific as possible. We tried to tell the physicians what kind of specimens to collect, how to collect them, where to send them, how to send them. This was really love's labor lost, because if you spoke before the Alameda County Medical Society or the San Francisco County Medical Society, everything was fine for a week or two, and then everything just collapsed to the previous state again. You didn't get very far with the house staff either because every July you had a new house staff come in, and you spent a lot of time telling them what was required, and then next year you had the job to do all over again.

Now in my earlier days, I guess I was really expecting too much, because to me virology was practically all there was to medicine. [laughter] But these people have a lot of other things to deal with, too, patients with physiological problems, endocrine problems, what else. So virology was just a side issue because it was still a clinical unknown.

Well, we did make some progress when virology became a more recognized field and people began to hear more about some of these newer diseases that were being turned up, for example herpes type I and type II. Now I can tell you that fifteen years ago I couldn't get any kind of monetary support to work on herpes viruses, the prevailing attitude being, "Well, it's not much of a problem. We see a few cold sores." This sort of thing.

But sitting at the forefront of a viral diagnostic lab, such as this one, which serves a big population, we began to see back in the sixties, I guess, when we had all this rebellion and strife on the U.C. Berkeley campus, an increase in genital herpes. Now mind you, this laboratory had been in existence since 1944, and we hadn't seen very much of this. All of a sudden the curve begins to rise up to the point it became explosive. Then, because it was sexually transmitted, there was all kinds of money available; all kind of basic research was being done; chemotherapy was being done on a grand scale, and everything that goes with it. You get all of the cream along with the dessert and the pudding and everything, to the point where this disease now is getting much more attention than many other diseases.

Well, another one which has just come to the fore is AIDS, acquired immunodeficiency syndrome. A reflection of the evidence thus far, although it's not entirely convincing, has been that it's sexually transmitted in the homosexual population. Of course there's

Lennette: some evidence now that it may be outside that population, too. That's getting a big chunk of the research money also. So we're having fads, as it were, and styles in virology, just as we do in other areas of medicine.

My stumbling block, my point of dissatisfaction, has been twofold really, as far as medical education is concerned. Most of these young people come into medicine with virtually no background in the classics. I think that's a real deficit. And I would hope that somewhere along the line universities would bring that back again. I believe every student should take a general education course, as I made my two sons do, although they are scientists, to get a good background in history, literature, languages, whatever goes into the classics background. You can sure see the ignorance among physicians today when they can't even tell you, or figure out, what some of the scientific terms mean. They have no sense of language roots or of etymology.

The other is the predominance of teachers in the so-called preclinical years, the first and second, who are so deeply concerned with basic research, they forget that the purpose of the medical school is to turn out practitioners of medicine, not high-powered researchers. In large part they forget it because the greater proportion of teachers in the basic sciences is at the Ph.D. level. It's not the M.D.; it's the Ph.D., who has no awareness of what goes on clinically, who has never seen or treated a patient. And this carries over to the very basic things, like DNA and RNA and the genetic code. Students are exposed to a great deal of this. This molecular biology is being pushed down into the college and high school level now. Nevertheless, while medical students today can tell you much about the organisms, the bacteria and viruses, whatever, from the DNA and RNA, the biochemical, and the genetic standpoint, recombination and translocation of genes and whatever, they learn, and hence know, very little about practical infectious disease problems.

Now that's becoming important. Why? Because with the introduction of penicillin right after the war, in the late forties or early fifties, when the wide spectrum antibiotics came in, physicians, but more appropriately, I guess, public health officers, felt that there were no more worlds to conquer. "Infectious disease is now under control; it's conquered, so let's go on to the chronic diseases." Which is what's been done.

Only now are we beginning to recognize, belatedly, that the antibiotics haven't done all that much for us. They've reduced the mortality, but they haven't reduced the morbidity. We have just as many common colds as we ever had before. We have just as many pneumonias as we had before. Maybe a little bit less now, with the vaccine. But things have not changed all that much.

Lennette: So the infectious disease person is coming back into his own. Mostly at the moment it isn't a separate field as it used to be. It's chiefly pediatricians and internists who do the infectious disease work. The pediatricians have never lost sight of the infectious disease problem. They have always been at the forefront, and the rest of medicine is catching up now, to the point where it's becoming a specialty again. It's a specialty, for example, because we have so many wide-spectrum antibiotics today that they're running out of our ears. Proliferation? We're into the third generation of the penicillins now. On top of these new antibiotics there are all the different brands differing because of different radicals hanging off the molecule here and there, so it takes a fulltime expert just to decide which one to use! Infectious disease as a specialty is coming into its own. Since these specialists now tend to work closely with clinical people, they have a much better perception today of how to obtain clinical material, how to send it to the laboratory, what tests to order, and what the answers mean.

#### The Training Program in Diagnostic Virology

Hughes: Did your training program in diagnostic virology turn out people who could then go out and direct a lab and see that procedures were done in the proper manner?

Lennette: No, not entirely. Early on we initiated training programs here to give people some background. Originally we gave a basic course three times a year. It ran for five weeks, and we would take fifteen to twenty people for each course session.

Hughes: Who were they?

Lennette: These were mostly people from public health laboratories, some from hospital laboratories, and not infrequently a postdoctoral fellow, either an American or a foreigner who happened to be here for a year's training, or perhaps only a six months' training. The classes were always full. And they still are every time we offer the class. We only give it once or twice a year because of the restriction of funds, and we can't take any more than about twenty people. But we do have a regular training laboratory set up downstairs, shared with the Microbial Diseases Laboratory, which puts on its own training program and workshops there. The teaching lab is down on the second floor of the Infectious Disease Wing, and is next to a lecture room with all the requisite projection equipment. It's a beautifully equipped teaching laboratory. It's unfortunate that more people don't know about it. Well, maybe it is fortunate that they don't, because we could never handle the requests that would come in.

Hughes: Was that, in the early days anyway, a major avenue for learning diagnostic virology?

Lennette: Yes, it was, in two ways. Number one, to train people. It gave people the flavor of virology, so that when they went back to their own institutions, they would know about virology a little bit better, having had some firsthand experience. And secondly, it interested some of these people in going into virology. Mind you, people didn't come already indoctrinated in virology. We had to train our own staff. In the early days, I would say the first ten, twelve, fifteen years, all the people on the staff who were appointed at the technical level had to rotate through the different units of the laboratory--virus isolation, virus identification, serology, whatever--so that when they finished, we could move them anywhere that we needed them in the laboratory. Otherwise, we would have had six people sitting in one laboratory unit with very little to do, while four were in this other laboratory unit just overburdened and could hardly keep up. We could assign people back and forth.

#### The Impact of State Funding Cuts

Lennette: Then when the Reagan administration came in Sacramento and decided to cut budgets and so on, we began to feel the impact; we couldn't maintain our teaching program; we didn't have enough staff. You see, to rotate people, you've got to have one or two extra people to make up the deficit, because the person that comes in doesn't have any background except for that four or five week course. So during that year of being on the staff, he has to rotate in order to pick things up. You've got to have somebody to back him up. So when we lost our two supernumeraries, we couldn't function quite as well. We're paying dearly for these budgetary restrictions.

And then, of course, you have to remember the state government today is run primarily by bureaucrats and attorneys and social scientists out to remake the world.

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So to balance the budget they'll cut here, there, and the other place without knowing what an operation requires, what its purpose is, and what an impact a cut will have. The easiest way to balance the budget is to just take out one big chunk. Instead of diddling around with forty-seven items, all with a small amount, and adding them all up and coming out to seven hundred thousand dollars, just take one big item and knock out six hundred and fifty at a crack. That perhaps happens to be a big piece of technical equipment which is needed for air pollution studies. Take that out of your budget, and you're dead! These political appointees and

Lennette: bureaucrats are still living in an antediluvian age. They forget we have a modern, technological society. Sometimes I accuse them of feeling that we should feel very fortunate to have adding machines and typewriters rather than just the goose quill pen, abacus, and a green eye shade.

And I say that very feelingly. Here's the sort of stupidity you contend with. They want to save money, so they just cut back on travel. Nobody can travel out of the state without permission of the governor's office, or as the case may be, through the administrative offices of the department in question. But the cut is such a blanket operation that it affects not only employees whose travel is supported by state funds, but those who use federal money. The stupidity lies in the fact that the money has been allocated by the federal government, let us say in a research grant, for the travel of the principal investigator who got the grant, so that if the administration says nobody can travel, whether it be state or federally supported, what are they doing?

Number one, you don't travel, so the money isn't used. The money sits there. Comes the end of the fiscal year, the money goes back to the general treasury of the United States. The State of California doesn't get to use it, and the granting institution loses it, so nobody profits. But the thick skulls that predominate to make such regulations just have it their way.

Now even worse is when you have federal employees assigned to this department to work in the field, to help out on control of sexually transmitted diseases, or under the old VD [venereal disease] program. They are called back by the feds. The Center for Disease Control says, "We want all of our people to come to Atlanta. We're going to have a one-week orientation meeting." The administration says nobody can travel. They don't even pay their salaries! And we've got forty-five people in this building who are working for the federal government, but they're assigned--they're seconded, as we say--to the State of California. And yet the birdbrains up at Sacramento wouldn't allow these people to go back to Atlanta or elsewhere as requested by the federal agency that pays their salaries!

Hughes: Well, getting back to the early days, I found some figures about the number of tests. In 1946 the Virus Lab performed almost six thousand tests. By 1949 you were performing over seventy-three thousand tests, which is quite a rate of growth. I was wondering how you coped with that tremendous increase in volume?

Lennette: We had staff increases.

Hughes: And space increases, too?

Lennette: Not so much space, but staff. When you're dealing with the kind of people I mentioned to you in the last two breaths I took, the arrant stupidity that you have to put up with in Sacramento (from whence all blessings flow), you learn to compensate for it by doing other things. As far as space is concerned, you plan for as much as you can get into the building, and you do that with two considerations. Number one is the safety aspect. Maybe you can put six or eight secretarial or business staff into a small office and get away with it, but you can't put that number of benchworkers in the laboratory in that same space, because then you have a problem of disease transmission and hazards. You've just got to give these people enough space.

### Designing the Virus Laboratory

Lennette: We had to design the Virus Laboratory when this building was laid out in 1949. I think I told you the background of this building-- it was put up with money that was appropriated before World War II! So when we put this building up, we thought that we were allowing for enough lab space, and we were. We moved in; we had enough space, except what the administrators and the architects took away from us. By the time we were ready to move in, it was obvious that the whole department wasn't going to fit in, so how do you suppose the allocations were made? With a blue pencil. You just take a blue pencil and you draw the outline: a piece of the wing is going to be administration, and the rest of this is laboratory, and you can have it.

We moved in here, and that meant we had to remodel at the last minute. We had to remodel the front part of the laboratory leading into the main building, to put another airlock in, because now our offices, which were planned to be outside of the laboratory proper, were inside the laboratory, and we had to separate that from the infectious disease area, otherwise none of the public could come in. So we had the expense of two airlocks rather than one, the cost of redesign, and the loss of valuable laboratory space.

If you'll go back to the original 1949-1950 plan, the building is the way it was planned at that time! It wasn't built that way, but it is now the way it was planned. [laughter] They had to get back to the nitty gritty and the fundamentals. We had very narrow doors at the Acton Street laboratory. I compensated for that by putting in forty-two inch doors in the main building here. I wanted large elevators that could take large equipment. Well, our omniscient architects and engineers felt this wasn't necessary, and so didn't put them in.

Lennette: So what do you suppose we do now? When a big piece of equipment won't go into the elevator, we just call up a rigging outfit with the huge rig and a dozen men take out one or two windows and lift everything up and into a lab, put the window back in, and re-concrete it. It's the cheap way to do it. Nobody in Sacramento ever looks at the final cost.

When I designed the so-called Infectious Disease Wing, we got a much bigger elevator. Not entirely what I wanted. Now we have a nice piece of equipment for which we just paid thousands of dollars. It's a liquid nitrogen tank. Each such tank will replace three of our dry ice boxes, but they measure ninety-five or ninety-six inches wide. There's no elevator that will take it in this building. So we now are confronted with the dilemma, how do we get this thing in without cutting it in half with a torch?

#### Types of Diagnostic Tests

Hughes: Well, with this expansion in the number of tests, were you also expanding the types of tests that you were able to do?

Lennette: Oh, yes.

Hughes: Can you give me an example of what sorts of tests?

Lennette: For example, when poliomyelitis came along, we didn't have any test except the neutralization test in monkeys, which is very cumbersome, or the complement fixation test, which Schmidt and I devised, and that isn't all that sensitive a test. Dr. Huang, who had been working with Claus Jungeblut at Columbia University, had devised a technique whereby evidence that the virus was growing in a cell culture was the failure to produce an acid that changed the color of the dye from a magenta to yellow; the virus kills the cells and so no acid metabolites are produced. But the method never worked very well, because there was no way to quantitate the cell content so that the number of cells would be uniform per well in the tubes (later micro-plates) and between tests. Then Jonas Salk and his colleagues came on the scene, and were able to work out--now this is a different era, too, about twenty years later--a method. The work of John Enders on cultivation of viruses in cell culture made this possible. So we had a pretty good metabolic inhibition test, which was added to the armamentarium.

Lennette: And we had in addition the hemagglutination inhibition test, which was devised by George Hirst, an outstanding investigator in influenza, not only from the medical side, but also from the very basic genetic side. He was one of the very first viral geneticists. Superb scientist and teacher.

So we had a metabolic inhibition test; we had a hemagglutination inhibition test. About 1940, a chap by the name of Albert Coons at Harvard--he was a young instructor--was working with immunofluorescence or fluorescent techniques, to hook a fluorescent dye onto an antibody molecule, so that when it combined with its corresponding antigen and was looked at under the microscope using ultraviolet light, it would fluoresce. A rather crude technique, but an important principle. This was worked over by a number of laboratories, and eventually developed into quite a technique. It's very widely used today, having become a standard method.

Then came the counter immunoelectrophoresis test, followed by others such as passive hemagglutination, radioimmunoprecipitation, enzyme immunoassay(ELISA), etc. Thus, over the years a number of tests came along.

Hughes: Now were you modifying these? Weren't most of these tests developed for a very small-scale operation?

Lennette: Yes. Here's the sort of thing that would happen: People working in the Z laboratory at X university would develop a test. "Gee, this looks pretty good. We've got some mouse brain here that we're using as the antigen, and we could put this stuff together and see what happens." And they do a lot of animals--maybe ten, twelve, fifteen animals. It seems to work pretty well. And then they get clinical material from half a dozen cases.

I can remember one paper described some twelve or fifteen cases of primary atypical pneumonia put together over a matter of several years. We were seeing several hundred a year, and we didn't think that was enough to publish a paper! Anyway, this is the kind of thing you contended with.

Now the real proof of the pudding is, what happens when you apply a test to man? How does the test function? Number one, is it sensitive? Number two, is it specific? And that's more important. Then you've got to study enough patients to be statistically sure that your test is diagnostically meaningful, that you're getting the true picture, that you're not getting false positive results, or on the other hand, false negatives. And this takes a little doing. It's a statistical thing. You accumulate enough cases; you can tell statistically that the test is worthwhile. That was our function. And we could do dozens, scores or hundreds of patients before we published a paper. If you will look at the papers out of the collected publications from this laboratory, you'll see that they're all based on big numbers.

Hughes: Yes, I noticed that.

Lennette: And that's how you make it meaningful. So that was sort of our mission, to say, "All right, fellows, this is fine, but does it really work when you get down to the nitty gritty of clinical medicine?" The laboratory is known for that approach. A lot of these things were proved. On the other hand, the laboratory was amongst the first in a number of things.

We were the first to show the existence of nonparalytic poliomyelitis due to other viruses, for example, mumps. Up to that point there might have been some small suspicion that mumps could produce a disease resembling poliomyelitis, but there was no proof. We did a whole series of cases which showed that other agents can produce a nonparalytic, or even polioliike, disease. This is why I mentioned earlier that you have to be sure the test is specific and, when done adequately, the results are meaningful. Then you can begin to separate out true poliomyelitis from other conditions. Until you can do that, you just have a hodgepodge of cases of varying etiology. You're throwing everything into the same basket.

#### Diagnostic Virology Laboratories Elsewhere

Hughes: Let's broaden the scope a little bit. I'm curious about diagnostic labs elsewhere. The first one that I know of is the Influenza Research Lab, which Clara Nigg founded and directed for about four years, between 1937 and 1941, and that was part of the State Department of Health in Minnesota. But that isn't really a counterpart of what you were trying to do, am I not right?

Lennette: No, it wasn't a counterpart

Hughes: They were strictly concerned with influenza. Within that scope of influenza, were they doing something similar? Did they have physicians out in the field who were sending in specimens?

Lennette: No. Well, they did when Rickard was there. Elsmere Rickard was a field man, a very good epidemiologist. He had a flair for seeing cases out in the field, getting blood and other specimens from patients, and so on. But the emphasis was mostly on the epidemiology of influenza. And that was true because we didn't have any tests, really, for the other respiratory diseases. Well, except for bacterial. We didn't have any for viral.

Hughes: Then another one, of course, was Francis' lab at the University of Michigan. But that again was focusing on polio, was it not?

Lennette: Well, before that it was influenza.

Hughes: That's right.

Lennette: Yes, it started out as an influenza and respiratory disease study, because he was trained at Yale under a very famous respiratory disease specialist, Y. Kneeland, Jr. From Yale, Francis went to the Rockefeller Institute as an independent worker on respiratory disease, so his interest was entirely in respiratory diseases, the common cold, for example. Then when influenza virus was discovered in Britain by [Sir Christopher] Andrewes et al., he was induced to move over to the Rockefeller Foundation Labs to work on influenza. This is early 1930s, when all of the research and studies being done in virology were being done in animals. This is about the time the embryonated egg appeared on the scene. I think that came about 1936, '37. Animal work and egg work were fairly expensive, and the foundation was one of the few wealthy enough and willing to support it. They had enough money to put into it.

So Francis was induced to come to the Rockefeller Foundation, where he and Tom Magill worked on the epidemiology of the disease, the passage of the virus, its properties and characteristics, use of viruses to make vaccines. He built a whole infrastructure, he and Magill. Just before the entry of the United States into World War II, Francis was appointed to the Armed Forces Epidemiological Board and chairman of the board's Commission on Influenza. About 1939, Francis went to NYU as chairman of microbiology. Salk came there as one of his students. Then from there Francis went to the University of Michigan as chairman of epidemiology in the School of Public Health and took Salk and some of the others with him. He also worked on influenza in Michigan until the polio foundation came along and induced him to get involved in this. Firstly he was involved as a consultant, I guess, and then he actually got into the mechanics, the fieldwork, also epidemiology and laboratory work.

Hughes: And of course eventually he became director of the Salk vaccine field tests.

Lennette: Yes. He was very competent to work on a big scale, because he was one of the few people that could handle a big project.

Hughes: But again, that operation isn't really comparable at all to what you were doing out here.

Lennette: No, ours was unique.

Lennette: Most physicians who pursued a laboratory career never did enough postgraduate clinical work to make them eligible for a license to practice. In other words, they hadn't interned or they dropped their clinical interests. Well, I never lost that interest. I still have my license to practice medicine. I used it all the time as a threat, too, so if anybody threatened me, I would say I could always go across the street and hang out my shingle. [laughter]

I kept my clinical interest, and I also kept a basic science and an epidemiology interest. In reality, I was trying to cover too much ground. Maybe I should have stayed in a department of medicine and placed my emphasis on the laboratory. This is retrospective.

Why the flavor of the laboratory here is so different is because of my interests. I returned to Berkeley in large part because Q fever had just come on the scene in southern California, and I was anxious to jump into this. I didn't know, nor did anyone else, that this was essentially a bacterial disease, as it were--the agent was recognized as a rickettsia. So I was all set up to come here and work on Q fever, and was given carte blanche, which I always had before. Nobody ever told me here in this hierarchical structure of the State Health Department what I could or could not do. There's no doubt I had a completely free hand. And I must say that that's unusual, except perhaps at a university. Nobody ever questioned what I was trying to do. They took it for granted that I was trying to meet objectives that were the objectives of the Department of Public Health. I returned that trust. Everything done in the Virus Lab was public health oriented, and this philosophy filtered down to my professional staff. As long as a project or study involved something that was a problem in public health, I didn't object. Sometimes we'd get involved in some pretty basic and fundamental research, not because we were trying to enter that field, but because there was a hiatus in knowledge. Nobody else was interested in providing the information to fill the gap.

Hughes: Getting back to the diagnostic labs, I also read something about a diagnostic service founded by George Hirst at the Rockefeller Institute which collaborated in some way with the Health Department of the City of New York, and that was founded in 1947.

Lennette: That's the Public Health Research Institute.

Hughes: That's one and the same?

Lennette: Yes. It must be, because I don't know that George had any contracts. George was with the Rockefeller Foundation at the same time I was. The lab staff was John Fox, George, myself, and a few others. I had just come back from Brazil. I already had been given the warning that when Wilbur Sawyer left--he was the one who started a

Lennette: lot of the influenza, hepatitis, and other work--and right after George Strode came in as director of the International Health Division, that the emphasis of the division would change, that there would be more emphasis and programs on agriculture--out of that decision came the Green Revolution--and less on medicine.

I remember when [Edward C.] Pickels came to the front office and said he had had an offer to leave. John Fox also had had an offer. Both were told to accept, with no attempt made to keep them. They wouldn't be dismissed or dropped; they could retain a position on the staff. But if something better came along, they should feel free to accept. The advice was, "Take it, because we are going to get out of the medical sciences." This was all open and aboveboard. We're going to change our emphases. If you don't want to go in this direction--and I don't know where an M.D. would go in agriculture--just change your direction and leave.

So about that time, the Public Health Research Institute, I guess, was looking for a director. The institute had been founded by Ralph Muckenfuss, director of the New York City Health Department, and whom I knew from my Washington University and St. Louis days. They'd had a director or two after that, and before George. George went to the Public Health Research Institute of the City of New York as its director, and completely changed the direction and flavor of the research program.

The money to run that shop came from the fees charged for doing tests on syphilis and gonorrhea, but mostly syphilis Serology on syphilis in those days was a big operation. They got two dollars per test; they were doing pretty well from the standpoint of a budget.

But what I could not fathom was how they could justify a lot of the research that was being done on other diseases, and especially at a very fundamental level. Had nothing, except very indirectly, to do with clinical medicine or even epidemiology or public health. The emphasis was on biochemical and genetic studies of viruses, a forerunner of the dawning era of molecular biology.

Hughes: But there were no questions on that point, as far as you know?

Lennette: Ostensibly not. I don't know what the background is, but I know that I often questioned the programs myself. This is not to say that the programs weren't any good. It was a good overall program, because out of that came quite a few very well known and recognized, even renowned, scientists today. These young fellows, carefully chosen, really made the grade under George's teaching and research. But you were supporting an institute whose objective was... It

Lennette: would be just like my doing very basic and fundamental research in this laboratory, which isn't what the legislature or the department wants, because it isn't what the health department needs; they need the sort of thing we were doing. However that may be, the Hirst group quickly gained recognition as being a fine group of scientists. There's no question about that. But it just didn't have much obvious relevance or pertinence to the practical problems of the City of New York.

Hughes: So it was another research group, really.

Lennette: Well, yes. But this is early on, you see. This is back now in the forties, early fifties, and molecular biology was just coming in to the fore. So George Hirst was really right in the forefront of what was going on in biology. He was on the cutting edge.

Hughes: What about Werner Henle's lab at the University of Pennsylvania?

Lennette: A fine lab. Has been over the years, and in my estimate, has never gotten the credit that it so well deserves or merits. The Henles came from Germany in the early 1930s, settled in Philadelphia, and both accepted positions at the Children's Hospital. The laboratory was in the basement of the hospital. Dismal place. All the sewage lines ran overhead through the place, and they were dripping. You didn't know whether it was sewage or whether it was just sweat coming off the pipes which were exposed. Both he and Gertrude (better known to all as Brigitta) were in that basement for some years. They did a fine job in the early days on influenza and also on mumps.

Hughes: Diagnostic?

Lennette: It was mostly research, but they did have a diagnostic laboratory on the side. One of the early directors was Michael Siegal, who later became chairman of microbiology at the University of Miami Medical School and who is now chairman of the department of microbiology at the University of South Carolina College of Medicine at Columbia, S.C.

The other one was Klaus Hummeler, a German colleague of Henle's, who is now the director of research for the Children's Hospital of Philadelphia. He was one of the pioneers in operating a viral diagnostic laboratory. They ran a good laboratory, but nothing on the scale of ours. You see, we covered the whole state. They covered just the metropolitan Philadelphia area.

Hughes: So the Henles' lab started before the war, you think?

Lennette: Yes. It was pretty much a local operation. It wasn't very large, and served primarily the Children's Hospital, which housed it.

Hughes: Does it still exist?

Lennette: Well, I think it does now. I think Stanley [A.] Plotkin, who is there now, revived it, and he and Harvey Friedman operate it jointly. Friedman spent about three months in this laboratory--he is a young pediatrician and went back to run the laboratory. But again, I think their laboratory is aimed mostly to serve the medical complex, that is, the Children's Hospital, and the University of Pennsylvania Hospital, which is just around the corner, and the Penn Medical School. But the Henles had a very fine research lab and of course that spilled over into this diagnostic lab.

Hughes: Was there any other group doing diagnostic work in the early days?

Lennette: Well, it all depends on how you define it, I guess. Everybody did a little bit, but it was pretty trifling. And it was not the primary endeavor. It was more of a side issue.

Hughes: How did other public health departments function without a diagnostic service?

Lennette: They didn't. You have to remember that California for years was a leader in many fields and was an outstanding department of health. It was unquestionably the finest health department in the country until the Reagan administration came in and politicized things and it began to fall apart. And what Mr. Reagan started, Mr. Brown finished. So we're way down on the totem pole now scientifically.

Hughes: You mean it was political appointments?

Lennette: Political appointments, interference with the operation of the laboratory. Mostly political appointments. Some of which were very unfortunate. People who were not really interested in public health, but more interested in sociology, social reform, MediCal, etc.

But despite the fact that the scientific endeavor has been crippled and never has found very much support with either the Reagan or the Brown administrations--there was no discernible difference between them--the scientific part of the department, the laboratories, have done very well, are still recognized as outstanding. Take the Air and Industrial Hygiene Laboratory. It's an internationally known laboratory, with visitors passing through all the time, giving seminars. It's just like a university department. The Virus Laboratory also has a whole string of visitors coming through, for training, for seeing how we do things, spending a few months with us on research projects, etc.

Lennette: But the laboratories really have a very low visibility in Sacramento. Most people there don't know we exist. Perhaps that's a blessing in a way. If they did, why they'd probably cut the ground out from under us. But we're just as pleased to have low visibility at this time.

Hughes: Did any of these other institutions that we talked about have training programs in diagnostic virology?

Lennette: No, not that I know of.

Hughes: So if you wanted training in diagnostic virology in the fifties, the only place you could really come was here?

Lennette: So far as I know. Well, other labs might have room... Somebody would write in because he knew the director of the laboratory; the chairman of the department would like to come out and spend three months or six months; you know, on that basis. But nothing formalized the way ours is. A possible exception was the Center for Disease Control in Atlanta, which began to set up lecture and lab courses in the 1960s--perhaps in the late fifties--for health department lab people of various states.

### The Early Years of Diagnostic Virology

Lennette: We have virtually written the books on diagnostic virology. There was no such field before this laboratory existed. We had to learn by example, by experience, sometimes bitter experience. We found that everything we read in a standard academic textbook of virology was not necessarily so. We learned that a virus freshly isolated from man or animal did not necessarily behave like the virus strain that we maintained in the laboratory, so-called tame virus, which might have been passaged through animals or tissue culture for generations.

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Virologists had to recognize that by transmission of a virus from animal to animal or from culture to culture over a period of time, what we ended up with through a process of natural selection or genetic selection was a virus adapted to growth in a new environment. A population of viruses is no more homogeneous than the human population; by passage, one culls out all of the inhomogeneous particles and leaves behind those which survive and so grow well.

Adaptation of influenza virus in the egg is one good example. It takes weeks, perhaps months, to adapt the virus to growth in this strange environment. Finally the virus takes off and grows like mad. Here we are dealing with an artificial animal or growth system, one that has nothing to do with what happens in nature.

- Lennette: But we had to learn that. So, as we began to publish papers, we began to point out these discrepancies between what some international authority on virology says in his chapter in such and such a renowned book; that it wasn't so. We also began to train our lab technical staff to recognize that there were differences in behavior between wild and "tame" viruses. Then, too, we had to make our own diagnostic antigens. We had to make our own immune sera. There was nothing that you could buy. We tried to get industry to make reagents. They weren't interested. "There's no demand for this stuff, Doctor, why should we spend our time and money making something that nobody wants?" It was catch-22. We didn't use the term catch-22 in those days; we just said, "Where do you cut into this circle? Because if you don't make it, nobody can get it to use. If nobody uses it, you won't make it. If it were available, maybe it would have a good market."
- Hughes: When did tissue culture equipment begin to come in?
- Lennette: Tissue culture really took off in the early fifties, after the work of [John] Enders and [Thomas H.] Weller and [Frederick C.] Robbins in '48.
- Hughes: But you were still having to make all your equipment at that stage, were you not?
- Lennette: We had to design racks to hold culture tubes, bottles, and so on.
- Hughes: What about the cell lines themselves?
- Lennette: Well, we had to learn how to handle those, not only from the standpoint of microbiological sterility, but also to prevent cross-contamination.
- Hughes: Would you get a starter, or whatever the term would be, from another lab?
- Lennette: Yes. Cell lines and cell strains were freely exchanged between laboratories.
- Hughes: Nowadays they're commercially available, are they not?
- Lennette: Sure. At that time, they weren't available. They're commercially available now because there have been enough laboratories set up to do this kind of thing. We have always told industry, if you have the reagents, people will use them. Now where's a small hospital up in Burning Stump, Iowa, going to get its tissue culture material? They're not going to keep a bunch of rhesus monkeys around at seven hundred dollars apiece and sacrifice one to make two thousand tubes of monkey kidney culture, most of which they'll throw away, because the cells won't keep. So they're going to have

Lennette: to buy their cultures as needed. And that's how the industry got built, because there was a demand for cell cultures and reagents and culture media.

Now when you get to diseases like herpes genitalis or cytomegalovirus, and because of the AIDS fear, there's a big market. The pharmaceutical companies will go all out to make these reagents because they can see where the dollar is. But for something for which there's little demand, or for something which is esoteric, they won't lift a finger.

Well, so they're out to make money. The antigens and antiserum they don't make are the counterpart of the so-called "orphan drugs" which are made under federal subsidy because the market is too small. In California, fortunately, we supplied many of the local public health labs with reagents to get them started. And then it got to the point where we were doing what you might call quality assurance, to be sure that the reagents they bought, whenever they could get them commercially, were up to snuff. Some of that early commercial stuff was pretty bad. So industry learned that there were checks in this state that would protect the smaller laboratories.

Then the hospitals began to get into diagnostic virology. Now we have hospital virus laboratories which say they've got a diagnostic service. We say, "Now, then, what do you do?" "Well, we do herpes genitalis and hepatitis B, and we do cytomegalovirus." That's where the bucks are. They don't do anything else! Sure, they just listen for the cash register to ring.

Hughes: That finishes my questions about diagnostic virology per se. Is there anything else?

Lennette: Well, that's getting to be a big field now. It's opened up, because a lot of these tests were feasible. I've spoken sort of disparagingly, I guess, of the molecular biologists, molecular virologists. Yet I have to acknowledge that they gave us a lot of the new techniques and made possible many of these tests. If it hadn't been for that, I guess we would still be sort of lumbering along. Tissue culture, the embryonated egg, the ability to purify antigens, the use of clear tissue culture fluids for the production of vaccines, have been a big step forward. Some of these techniques, which have gone into the second and third generation, hold great promise. These have all contributed greatly, so that we have a variety of tests, and we have found that with some viruses certain ones do better than others. So we're learning.

Lennette: But not much is going to come out of these hospital laboratories, because hospital laboratories, with some exceptions, are not research oriented. You take a laboratory like Mt. Zion across the way in San Francisco, which is run by Dr. Larry Drew. They're interested in clinical research, and they're also interested in laboratory research, so they give diagnostic virology lots of support in how these tests and exams behave when you're dealing with large clinical populations. That is a much more reasonable way to test a new procedure than in a university hospital. That's a dead end when you get to the university hospital. They see all the arcane and exotic cases. They don't see the run of the mill patients and conditions a primary care physician does.

New Directions in Public Health and Diagnostic Virology

Lennette: The next step unquestionably is going to be commercial laboratories doing viral diagnostic work. I think the department of health laboratory, such as this one, has pretty much seen its day.

Hughes: Why is that?

Lennette: Commercial laboratories are on the horizon, and government labs will fade out. I also feel that schools of public health have passed their heyday, and they too will pass on. My colleagues across the street at the U.C. School of Public Health I'm sure won't agree with me; they see a bright and rosy future for schools of public health--but not what I call a school of public health. Because after all, schools of public health were brought in, oh, back in the twenties, at the instance of the Rockefeller Foundation again, to train people in public health methods--epidemiology and statistics, and so on. They served a need to fill gaps in medicine, and they served their purpose. Public health is a bastard discipline, a mixture of everything, a hodgepodge of disciplines that meet a need. Today, just throw a lot of odds and ends together and you have enough material to give somebody a degree. That's not how they started out.

Now the schools of public health are what? Administration, social work and whatever. There's virtually no infectious disease, very little epidemiology, and very little that used to characterize a school of public health. So the true school of public health is just disappearing.

Now when bacteriology first developed as a discipline--I'm giving my own opinions now; I don't know whether other people would buy this or not, although some of it they would probably have to agree with--one of the major places where it could be taught and put to practical application was at schools of public health, or schools of hygiene, as they were known in Europe.

Lennette: Now the schools of hygiene in Europe were a different kind of cat from the schools of public health here. They were all tied in with the university to begin with, with its medical school, so the professional staff of the school of hygiene also had an appointment on the faculty of medicine, and vice versa. So microbiology was taught in such hygiene institutions, and that's where most of the hospital material came from. There were very few laboratories that could test--well, that were routine diagnostic laboratories. Eventually bacteriology in this country was incorporated into hospital laboratories, actually into the discipline of clinical pathology.

Over the years much of that microbiology emphasis has been lost, so that clinical pathology today is mostly biochemical tests for various things. But microbiology has suffered because the young professional out there with a bachelor's degree is doing the microbiology, and if he gets into difficulty, who is he going to go to? He's going to go to the pathologist in charge, who's got even less background probably than he has, because his emphasis is in chemistry and in surgical anatomy. That's where the big effort goes.

So the kind of bacteriology which is being done--or parasitology, too, for that matter--is fairly straightforward and routine. They don't get into too many difficulties, so there's no real reason why it should be done in the health department, except if a laboratory in the health department is used as a reference laboratory, or a resource where you can send material which you can't identify and have that lab do it. This is what our Microbial Diseases Laboratory does downstairs. They don't do any routine work for the hospitals or for the local health departments.

So this laboratory, the Virus Lab, is going in the same direction. As we farm out a lot of our routine work to the local hospitals or local public health labs, we have time left over. Well, you can do two things. You just close out the shop, save the taxpayer money, or you can divert that effort into support of epidemiologic studies and investigations for the infectious disease people, which is what we're doing now. Or use it for training, which is also what we're doing, not only in this building, but we have teleconferences statewide. We just select ten or fifteen different health departments, and then tie them all in together by telephone. We send them a syllabus beforehand with all the tables and pictures and graphs in it. Then, at the telecom we have some staff member lecture, just the way you're sitting there, with a microphone or with a telephone, and it goes to all these local labs. They just turn the pages of the syllabus, and they can go right along with the discussion. They can ask questions, and everybody else can hear. That's one way we're keeping the local labs abreast of developments.

Lennette: In addition, we put in what we call the wet lab here in this department. They come in and work right at the laboratory bench and do the viral identifications. For our part, if somebody isolates a virus and can't identify it, we'll identify it. Pronto. None of this fooling around that you get in so many university setups, because we're geared to do large volumes of work expeditiously.

Research on Nonpolio Enteroviruses

Hughes: Shall we move to the nonpolio enteroviruses? In 1958 you received a twenty-year grant from NIH. What was the purpose of the grant?

Lennette: The grant was really sort of an umbrella grant, because it covered a number of efforts. It covered research that Dr. [Robert] Magoffin and I were doing on the enteroviruses. It covered the research that Dr. Schmidt was doing, and also that of Dr. Natalie Cremer and Dr. Jack Schieble. In addition, it supported the research efforts of some of our postdoctoral fellows. It also covered some of the work Dr. James Chin and I were doing at Fort Ord in the civilian population.

Hughes: But not the polio?

Lennette: No.

Hughes: You were still receiving money for that from the National Foundation for Infantile Paralysis?

Lennette: Yes, but just about that time, the polio foundation folded up, so that whatever we were doing on polio was really incorporated into the enterovirus studies.

Hughes: Was your effort on the nonpolio enteroviruses an outgrowth of the polio work?

Lennette: Yes, we had been through this business once in a different way. Back in the late forties, early fifties, we had a lot of cases of polio being reported to our infectious disease section, frank paralytic polio and nonparalytic polio. There was no way really to sift out what all these various things were. The holes in the colander were so big that everything fell through. There was no way to really strain them out by size and make definite etiological diagnoses.

Lennette: And then came the diagnostic tests for polio, first the CF [complement fixation] test, and then the metabolic inhibition test, which was the test par excellence. Much better than the CF test, which Schmidt and I had devised for determining immune status and for diagnosis. So we now had a good, specific test for polio. In addition to being able to isolate the virus from stool specimens, we had a test to follow the antibody response. Now we could really nail down, given the history of the patient, cases of poliomyelitis, paralytic or nonparalytic.

But when you did that, you still had a fair residuum which was negative by these tests. Now if you did the complement fixation test for western equine encephalitis or for St. Louis encephalitis, depending upon what year it was, you found a fairly appreciable proportion would fall into one or the other of these categories. Not every year, but periodically.

Well, the whole thing in a nutshell is that in the years when we had a great deal of poliomyelitis reported as paralytic polio, we had a whole lot of nonparalytic polio reported. Okay? In those years when the paralytic polio incidence was low in the population, we didn't have much nonparalytic polio. And then would come an epidemic, like 1952 or 1957, when there was a great deal of western equine or St. Louis encephalitis, but not much polio. So when we began to apply these tests, we found pretty soon that this big curve we had for nonparalytic polio was spurious, because it was a hodgepodge of diseases. When we really sorted out the western equine and the St. Louis, and later on, mumps, from all of this potpourri, we were left with a small residuum which was true nonparalytic polio, and moreover was a relatively small proportion of the total. I'm not saying anything about the other infections, because some of them would eventually turn out to be coxsackies or one or another enterovirus. In other words, we were seeing a clinical picture of nonparalytic disease that resembled clinical nonparalytic polio.

Contrary to that, we later began to see cases of mild paralysis--not began, really, because it began only when we started to look for it. It probably always did occur, but unrecognized. We began to look at this picture from the standpoint of what we already knew about nonparalytic polio and its etiology, and we saw some cases which had a paralysis, and much to our surprise, a fair number proved out as cases of mumps. Some were coxsackies. But applying the thirty-day rule that the National Foundation for Infantile Paralysis devised--does the paralysis persist or is it transitory?--most of these were transitory, so that by day thirty postonset most of the paralysis had disappeared or left only very minor muscle weakness. This gave us our first leads that there were other diseases that can closely simulate nonparalytic polio.

Lennette: We had been looking for years for herpes meningitis--another instance of how you are prejudiced. We had also been looking for LCM [lymphocytic choriomeningitis] virus as a cause of aseptic meningitis because we used to see a fair amount of meningitis. Well, in all the years that we looked for it, I don't think we found more than one or two cases. Finally, we got so tired running these tests, we decided we'd better look for something else. And that's when we began to look for herpes meningitis and mumps. And again, the herpes didn't amount to very much. But mumps was the payoff, because there were quite a few cases of those, again allowing for some of them being caused by enteroviruses. Mumps produced an appreciable number of cases. This is a matter, as it were, of serendipity. You look for one thing, and you find something else.

Albert Sabin published a paper about a year or two ago in which he reviewed all of the available data, much of it from this laboratory, and used it to support some of his own ideas of what he thought these diseases were.

Hughes: How did this relate to the Salk and Sabin programs of polio vaccination?

Lennette: It really had its start with the Salk program, because the National Foundation gave this laboratory the responsibility of doing all of the tests for the eleven western states, the idea being that every child that received Salk vaccine and then developed any kind of a weakness or paralysis or illness, stool and blood specimens would be sent to Berkeley. Then we would do the virus isolations to see what agent could be recovered, and also do the serology and see if there would be a rise in antibody. We were doing this on a huge scale, hundreds of tests a week. We began to see that a lot of these illnesses were not vaccine associated at all, that there were other disease agents involved. We didn't know what agents, because we were merely screening, but when we later began to look for some of these other agents, we found out that they were probably responsible for a considerable number of these illnesses.

Obviously, it was the Salk field trials, the vaccine trials, that set the stage for this major study. That was important, too, because if the vaccine was going to produce any reactions, we wanted to know what those reactions were. Is this going to produce paralysis? If a patient does have a paralysis, it is poliomyelitis or is it something else? That's how a lot of this began.

Hughes: You were convinced that these nonpolio diseases were not caused by any of the vaccination programs?

Lennette: Yes.

Hughes: You were looking and finding things that had always been there?

Lennette: Yes. We had to take a good look to be sure that the vaccine was not producing these reactions. We felt we were able to rule that out.

You see, that's the strange part, that all through this business, we didn't find any cases of minor weakness, or even paralysis, that we could attribute to the vaccine. Yet when the field trials were finished and the vaccine was administered on a large scale through immunization programs in the general population, we began to find paralysis following vaccination. Well, that's because pharmaceutical houses were now making vaccine on a huge scale, and some of them didn't have much experience of making the vaccine, which was to be produced to a set pattern.

You take Parke-Davis, which was in the program from the very first. Right at the start they knew there were problems, so they attacked them and eventually resolved them. But Cutter Laboratories wasn't apprised of the things that could happen, didn't encounter any obvious manufacturing or quality control problems, and very early ran into disaster.

#### The Identification of New Viruses

Hughes: In 1958 you reported what I believe is the first laboratory isolation of a new enterovirus. It was the Coe virus,\* and several others followed. I know about the Caldwell virus\*\* and the Price virus\*\*\* and maybe there were others as well. Can you tell me something about establishing a new virus? What the procedure was for naming it and having it accepted?



Lennette: Usually it's something like this: The virus is named after the patient from whom it is isolated. Most patients when you tell them about it are delighted to have something named after them. This is not the case with their activist friends. They think this is terrible. It's a violation of privacy, and there are regulations against invasion of privacy. You get into all that jazz. So as a result, now we end up using identifying initials, EC or OC or QJ or whatever.

Hughes: It's not very colorful.

Lennette: No, not very colorful. You can thank the bioethics activists for that. They're always screaming on behalf of some cause, and laying ground rules for other people to follow, irrespective of the detrimental impact.

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\*Edwin H. Lennette, Virginia L. Fox, Nathalie J. Schmidt and James O. Culver. "The Coe virus. An apparently new virus recovered from patients with mild respiratory disease." J. Immunol. 81(1958):452-459.

\*\*Edwin H. Lennette, Nathalie J. Schmidt, Robert L. Magoffin, and Anna Wiener. "Recovery of a newly recognized enterovirus from patients with aseptic meningitis." New Eng. J. Med. 266(1962):1358-61.

\*\*\*Edwin H. Lennette, Nathalie J. Schmidt, Robert L. Magoffin, Juanita Dennis, and Anna Weiner. "The Price virus. An unclassified enterovirus isolated from patients with central nervous system disease." Proc. Soc. Exp. Biol. Med. 110(1962):769-75.

Lennette: So the Coe virus came from a young recruit at Fort Ord who had a respiratory disease. If you have enough experience in the laboratory with tissue culture, let's say, and you inoculate such cultures with clinical material, oftentimes you can tell to what large group a virus belongs just by the kind of cytopathic effect it produces in the culture. You have to have considerable experience. I couldn't do this, but my staff in the laboratory does it every day. They can see the beginnings of something you can't even see. It's just sort of a sixth sense. Intuitively they know that something is happening to the cells.

Hughes: Now this is looking at the histological picture?

Lennette: No, looking at the culture itself, changes in the cells in the culture. Similarly, if they do fluorescent antibody studies trying to identify a virus, they can see changes where you or I can't unless we're doing this every day. Returning to cultures, just by the kind of cytopathic effect that is produced, you get a rough lead as to whether it's an adenovirus or a coxsackie virus, a herpes virus, whatever.

If it turns out that you think this is an enterovirus, then you've got a real job ahead of you. Which one of sixty some is it? You have to start weeding them out to identify the one at hand. But you get a pretty good idea of the virus and its type if you use the technique Schmidt and I devised, what we call the intersecting serum scheme. We use pools of sera. Did you see reference to that?

Hughes: Yes, I did. I was going to ask you about it.

Lennette: It's sort of like a square or a box. You have serum types along the top and serum types along the side, so that you have a mixture usually of two serums, (sometimes more, depending on how you set up your scheme). With a series of two serums per pool, going across and going down, you can determine usually in which tube neutralization occurs. In other words, out of all these tubes you've inoculated, the virus is inactivated by this one pool. You don't know which one of two viruses it might be. You then go back and check both and you get the answer.

Now if something is growing in that tube and none of these sera neutralize it, then you say, "Well, it's a virus other than an enterovirus; it may be a new agent." Then you start doing the tests to see whether you really have got a new agent. You make immune serum against it in an animal, and see how that serum reacts with all these other viruses.

Hughes: So it's a process of elimination.

Lennette: That's what it amounts to.

Hughes: And then once you think that you do have a new virus, what is the next step?

Lennette: The next step is, where does it fit taxonomically in the scheme of things? As I mentioned, Gilbert Dalldorf, who acted as the repository for coxsackie virus, crossed us up with the Coe virus because he didn't number all of the coxsackie A viruses sent him by the various research labs. He stopped with type 18 or 20 or something like that. We thought that since we tested for all eighteen known and numbered coxsackie viruses, and this one didn't fall into any of the group; it must be a new one. So we called it Coe. Actually, Dalldorf had already done more than the first eighteen, but there was no report of it.

Well, I told you how some time later Schmidt happened to be using Coe virus immune serum as a control in a gel diffusion study and found out that this serum neutralized her coxsackie A21 virus, so that raised the question of nomenclature. In essence, Coe virus and coxsackie A21 proved to be identical, and we published another paper to this effect.\*

Hughes: I believe there is a committee on virus terminology, is that not true?

Lennette: That's right. In this case neither we nor they had any choice, because the Coe virus, as we named it, had already been described as coxsackie A21. All we really did was publish to set the record straight. As a researcher, you have a responsibility. Some people don't exercise it, but when we reported finding a new virus, and it turned out that it was already known, then it was our duty to go back and say, "Look fellows, this is not a new virus. This is coxsackie A21 as described by Dalldorf at such and such a time." Except the rascal, he hadn't published it. [laughter]

Hughes: What about the Caldwell virus? In that case, once you published your paper, does the committee itself do any checking to see that this actually is a new virus?

Lennette: Yes. It is not unusual for several laboratories to collaborate on a problem.\*\* The Caldwell virus, which has now been renamed as echovirus type 31, was actually isolated by three different laboratories at about the same time, namely here in our laboratory, by Prebend von Magnus in Copenhagen, and by Herbert Wenner in Kansas City. Since Wenner's isolation of the virus antedated the other two, it was named after the Kansas City patient.

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\*Nathalie J. Schmidt, V.L. Fox, and E.H. Lennette. "Immunologic Identification of coxsackie A21 virus with Coe virus." Proc. Soc. Exp. Biol. Med. 107(1961):63-65.

\*\*Dr. Lennette added the following four paragraphs after the interviewing process had been completed.

Lennette: Another excellent example of a collaborative effort is that of identification and classification of a virus recovered from several epidemics of acute hemorrhagic conjunctivitis occurring over several years. This disease first appeared in West Africa, spread northward and across to the Indian subcontinent, and later appeared on the Asian mainland. The virus was responsible for the pandemic and for the millions of cases which occurred, in toto probably one of the largest pandemics of an infectious disease ever recorded. Four laboratories collaborated in determining the taxonomic position of the virus first isolated by Reisaku Kono of Tokyo--his laboratory, ours, Melnick's, and that of R. Sohier in Lyon, France--which was finally classified as enterovirus 70, a new immunotype. These same four groups collaborated in identifying and finally classifying another agent isolated from one of these conjunctivitis outbreaks, a virus which proved to be a variant of coxsackie virus type 24!

While on the subject of enterovirus 70, its high infectivity, or high contagiousness, is illustrated by the rapidity with which it spread in Africa and Asia. Yet despite this high infectivity, no cases of accidental infection occurred in any of the four laboratories which worked intensively with this virus. My point is that highly infectious microbial agents can be contained if proper laboratory safety precautions are strictly observed and followed, a point of which our nonmedical molecular biology friends ostensibly were ignorant, or how else explain the horrendous doomsday scenarios which poured forth in the early days of the recombinant DNA controversy?

Do you know about the Marin agent recently described from this laboratory? We saw it, using electron microscopy, in the stools of patients during an outbreak of diarrheal disease in a home for the elderly in Marin County. We saw the virus, thought it was a new agent, but couldn't grow it for the usual tests one does. So we sent some of our material back East to Albert Kapikian at the National Institute of Allergy and Infectious Diseases. Using his spectrum of immune sera, he agreed that the Marin agent was a new pathogen, heretofore undescribed. We don't know where this agent belongs taxonomically, just as we don't know where the unrelated Norwalk agent belongs. In addition to these causal agents of acute gastroenteritis, the newly-described rotaviruses are also offenders just as are some of the adenovirus serotypes.

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Hughes: This is all very recent?

Lennette: It's all recent.

Hughes: Do you care to say any more about the enteroviruses?

Lennette: You asked me about classification. There's an International Committee on Taxonomy of Viruses which meets every time the International Congress on Virology meets. This committee reviews all data for new agents, and even new data for the old agents, to see how they should be classified, and then reclassifies as indicated. Thus, there is a whole system of nomenclature based on the appearance of the virus, on its chemical characteristics, its physical characteristics, etc. Dr. Melnick does a great job as coordinator of the committee. So when we got a presumed new enterovirus out, we generally sent it to him for checks.

Reoviruses and Rex Spindlove

Hughes: Let me start out with Rex Spindlove, because reoviruses seem to have been his province. Am I correct in that?

Lennette: Yes.

Hughes: From what I can gather, Rex Spindlove came as a postdoc in 1962?

Lennette: He was a postdoc, yes.

Hughes: What was his background?

Lennette: I don't know whether he was at Logan or whether he was at Salt Lake City before he came to us.

Hughes: In microbiology?

Lennette: Yes.

Hughes: How did he get interested in the reoviruses?

Lennette: Probably because I gave the project to him to work on. [laughter] I don't recall.

Hughes: Not much was known about them?

Lennette: No. At that time, this was a relatively new group of viruses, which I thought might prove of medical importance. So Rex worked with them in the laboratory, trying to determine their characteristics, their nature, and their behavior in tissue culture systems. He found that infectivity did not necessarily relate to particle count. I think one of his most pertinent findings was the observation that if you put trypsin into the infected cell cultures, you increased infectivity. This was the first indication that the reoviruses have a double layer around them rather than a single layer. Trypsin digests the outer layer or coat and exposes the second one, which then makes the particles highly infective. This phenomenon of increased infectivity upon uncoating was

- Lennette: probably Rex's major contribution. Uncoating of the virus occurs within the cell after the cirion, the viral particle, has penetrated the cell.
- Hughes: I see. This sounds to me to have been very basic research.
- Lennette: It was very basic.
- Hughes: Which goes back to your original contention that you were pretty much allowed to do what you liked.
- Lennette: Yes. For instance. we were very much interested in the matter of infectivity. Under the electron microscope you see a lot of viral particles, and yet when you do infectivity tests, you don't get much of a titer, that is, a high, but variable, proportion of particles may not be infective. We found out in the case of adenoviruses, for example, that a lot of the viral particles aren't assembled properly. Nature isn't perfect. To compensate for the poor assembly work on polio virus, for example, infected cells make millions of particles, like an auto assembly line producing ten million wheels when all you need is a million. The excess is just junk, useless. These viruses are turned out in the same numerical fashion. Rex wanted to see what the problem was between infectivity and what you saw in the electron microscope, and trying these various techniques he found that pepsin and other proteolytic enzymes would remove the top or outer coat. Reovirus turned out to be a double-coated virus.
- Hughes: What about his work with reovirus antigen associated with the mitotic spindle? There were several papers on that.\* Do you remember?
- Lennette: Yes, I recall he was working with several antimitotic agents, for example vincristine, as well as several other anticancer drugs. He was studying the effects of these antimitotic agents on viral replication, because synthesis of reovirus protein, which occurs in the cytoplasm, is associated with mitotic structures, such as centrioles and spindles, involved in cell division.\*\*

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\*Rex S. Spendlove, Edwin H. Lennette, and A. Charlotte John. "The role of the mitotic apparatus in the intracellular location of reovirus antigen." J. Immunol. 90(1963):554-60.

Rex S. Spendlove, Edwin H. Lennette, Jean H. Chin, and Charles O. Knight. "Effect of antimitotic agents on intracellular reovirus antigen." Cancer Res. 24(1964):1826-33.

\*\*The foregoing paragraph was added after completion of the interviewing process.

Hughes: I think it was your son--could have been Nathalie Schmidt--who said that approximately ten years after Spendllove had begun this work, which was on the basic level, it suddenly had a direct clinical application in that infant diarrhea was found to be caused by a reovirus. Investigators then went back and looked at Spendllove's earlier work and used several of his techniques for studying reoviruses.

Lennette: Reoviruses have been associated with diarrhea or enteritis of children, but the causal relationship of reoviruses to human illness has not been unequivocally established. You may be thinking of the rotaviruses, which are related to the reoviruses, and are very important as a cause of diarrheal disease in infants.\*

With respect to the reoviruses, a lot of investigators have gone back and looked at his work for which, incidentally, he has received relatively little credit. He deserves more credit, because he really opened up that field. The use of trypsin or some of these other protolytic enzymes provided an important tool to study the molecular aspects of the reovirus genome.

Hughes: He was one of the first to do that then?

Lennette: He was the first. And other people came along and used the same basic techniques which permitted studies on the viral genome. The reoviruses today are used as a model to study the role of the various genes in pathogenesis, virulence, etc.

Hughes: He also had something to do--perhaps he devised it--with an immunofluorescent plaque technique? Do you remember that?

Lennette: Yes. He did the early work on it by using labeled agents.

Hughes: Now was this all a direct descendent of [Renato] Dulbecco's work? Dulbecco's paper on the plaque method came out in the early fifties.\*\*

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\*The foregoing paragraph was added after completion of the interviewing process.

\*\*R. Dulbecco. "Production of plaques in monolayer tissue cultures by single particles of an animal virus." Proc. Natn. Acad. Sci. USA 38 (1952):747-752.

Lennette: Dulbecco devised the plaque method for viral assay in cell culture. He used to do most of his testing with western equine virus. Why western equine, I don't know, but perhaps he considered it a good model agent. He got most of his starter cultures of virus from us. He would periodically write to us to ask for new viral cultures, leading me to wonder what's happening to this laboratory, they keep losing their western equine. We seemed to be just sort of a continuous source of supply. Well, actually that wasn't so. He was trying different strains and different batches.

No, what he had done was work out a very basic assay tool, very nice technique. He did for virology what bacteriologists had done for bacteria and for bacteriophage, and plaqued them out. The only way we could grow virus was to put a lot of test material into a test tube or flask with tissue in it and see what happened to the tissue. If it degenerated and died, we knew we had a virus growing, but when we had to quantitate it, we had to do just as we did in monkeys: use five tubes for a ten to the minus one dilution, that is, a one to ten dilution of the virus, then five tubes for one to a hundred, and one to a thousand, etc., and then compute a fifty percent endpoint from the final tests results.

He showed that the plaque technique is a much more sensitive virus-counting method, each plaque ostensibly representing one viral particle. He was able to work out the conditions under which plaquing could be done. You had to use the right number of cells in the culture; you had to have the right pH, and so on. He showed that you could titrate viral material in plates. If you got down far enough in a dilution serum, you could separate the viral particles; they would grow individually. Each viral particle would thus produce a clone just the way bacteria do. It was a real advance.

People have forgotten that he originated this method, because it's an everyday tool now. The graduate students don't go back more than three or four years in their background reading, and if you mention Dulbecco and some of this early work, they never even heard of it, never knew that he did it. Well, eventually he became a Nobel laureate. But he opened up a whole big area of the virus field with this technique. It's the most sensitive technique we have for quantitating viral particles.

Hughes: Did he get the Nobel for that particular work?

Lennette: No, it was for a lot of very basic contributions that he had made along that same line--no one single thing, but a whole variety of contributions.

Hughes: Well, that's all I had to ask about reoviruses.

Lennette: Check up on the reoviruses and let's find out what else was done. I never paid too much attention to reoviruses, because they didn't seem very important to human medicine.

Hughes: There weren't many papers on reoviruses in your bibliography.

Lennette: No, because what Spendlove was doing was in the pioneering field, and it was all hard, uphill work.

### Respiratory Viruses

The Armed Forces Epidemiological Board

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Hughes: Would you tell me how and when you became a member of the Commission on Influenza of the Armed Forces Epidemiological Board?

Lennette: Well, when I returned to Berkeley at the end of 1947, Monroe Eaton, who was the director of the laboratory here, had already left to accept a professorship at Harvard Medical School, and so, in effect, the laboratory had no representation on the Armed Forces Epidemiological Board committees, specifically the Commission on Influenza, because Eaton had been representing the laboratory. Hence I suggested to Dr. Thomas Francis, who was chairman of the Commission on Influenza, to appoint Dr. Gordon Meiklejohn to the commission. Meiklejohn was an assistant professor of medicine at the University of California at San Francisco, and had been working on respiratory diseases with Eaton. As a matter of fact, he was closely involved in work on the Eaton agent, as well as on influenza. In any case, Meiklejohn was appointed a member of the Commission on Influenza, and Dr. Francis appointed me an associate member because he felt that both of us should be on the commission. But Gordon was the most actively concerned with influenza, and I was more tied up with Q fever.

Eventually, when Gordon Meiklejohn left the Bay Area to become professor of medicine at the University of Colorado School of Medicine at Denver, I took over his position as a full member of the Commission on Influenza and served on that commission for many years. I was also a member of the Commission on Rickettsial Diseases because of the work on Q fever, so I was actually serving on two committees.

Hughes: That was also under the army?

Lennette: Under the Armed Forces Epidemiological Board. And the World Health Organization appointed me to two of its committees. One was a committee on viral respiratory disease, and the other was a committee on rickettsial diseases. So I had two appointments there.

Hughes: That all happened in 1948?

Lennette: Forty-eight with the AFEB and 1952 with the WHO. The Commission on Rickettsial Diseases was rather small because, as is usual in peacetime, nobody cares much about rickettsial diseases until we have another emergency or a catastrophe arises, and then everybody wants to get the talent on board to study the disease or do something about control. The number of people in that field has always been pretty small. That's still true today, as a matter of fact.

Eventually, through long service on these Armed Forces Epidemiological Board commissions, I was appointed president of the Armed Forces Epidemiological Board. The Armed Forces Epidemiological Board represented a cross section of investigators or scientists working in these various fields. A commission chairman might be a member of the board, but not generally, avoiding what today is called conflict of interest, I guess. You can't have too many interlocking directorates.

So I was on the Armed Forces Epidemiological Board for quite a while. The work under Meiklejohn progressed quite satisfactorily, then when he left--I don't recall the year, but it was somewhere around '54, '53 maybe--I took over the work on influenza, studying primarily influenza vaccines, and evaluating their efficacy. And as you know, it's very difficult to evaluate a vaccine in the absence of the disease for which it was devised. [laughter]

Hughes: I should think so.

Lennette: So we spent a number of fruitless seasons vaccinating thousands of recruits at Fort Ord, California, and yet the disease wouldn't appear, so we had no way to really evaluate the vaccines, although, on the few field trials that we were able to do, the vaccine seemed to be quite effective. The vaccines left something to be desired, but they were effective, crude as they were.

We were also concerned with studies on the etiology of the other viral respiratory diseases which occurred in large numbers at Fort Ord, and out of that came, as you may recall, isolation of the so-called Coe virus, which turned out eventually to be coxsackie A21. But aside from that, there were quite a few cases of adenovirus disease, types 3, 4, and 7.

Hughes: Were you from the very start aware in these military studies that there was something that was not a strict flu virus?

Lennette: Yes. We were just getting into the polio business, but we were aware that other things besides influenza virus were responsible for some of the disease.

Hughes: This was very early fifties, would you say?

Lennette: This was early fifties. Because we already knew about influenza A and influenza B, and I was part of the group that devised the nomenclature of influenza A and influenza B,\*we thought that the next virus would be C and so on. But we never got much beyond C. As a matter of fact, there's a question today whether influenza C virus is a true influenza virus. Taxonomically it may be placed elsewhere, so we have only two, A and B.

But adenoviruses were discovered by Maurice Hilleman's group at the Walter Reed Army Institute for Medical Research, and also by Bob Huebner and Bob Chanock's respiratory group at the National Institutes of Health, at about the same time. It was shown that these viruses were a cause of respiratory morbidity in the military. Other adenoviruses later were found to be the cause of morbidity in young children. That's the other, lower type. And we still have some types which we have not yet been able to associate with a disease. They may be involved in disease, but we haven't been able to tie them together.

Hughes: According to my notes, the adenoviruses were first isolated in 1953, and then only three years later an effective vaccine was produced. Wasn't that very quick? Does that tie in with the up and coming technique of tissue culture?

Lennette: Yes, I suppose you might lay it to that, but you're dealing with a different kind of a virus and one which isn't changing its personality all the time. Adenovirus type 3 stays an adenovirus type 3 pretty well, while influenza virus mutates. There are changes every year. They may be minor, or they may be of such a magnitude that you've got a whole new virus. So the adenoviruses, like the polio viruses, didn't pose any problem from the standpoint of stability.

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\*F.L. Horsfall, E.H. Lennette, E.R. Rickard, C.H. Andrewes, Wilson Smith, and C.H. Stuart-Harris. "The nomenclature of influenza." The Lancet, London 2 (1940):413

## Tommy Francis' Role in Influenza Research

Hughes: Could you say something now about Tommy Francis' role in establishing the protocol of these tests?

Lennette: You mean for influenza?

Hughes: Yes. And the second question would be, did he have any input into the adenovirus studies?

Lennette: Dr. Francis as chairman of the Commission on Influenza was a source of information for all the investigators working on influenza, because data used to funnel into his office, primarily through the military, which had laboratories all over the world. This was, you remember, at the time right after the war when we had a lot of troops stationed abroad. So he had a great deal of firsthand information, which he used to give us by telephone or by a round robin letter. Frequently by telephone. So we knew when influenza was occurring anywhere in the world. Of course, this was also tied in with the World Health Organization, which was also deeply interested, although it came into the picture some years later.

Francis' role was not to tell the commission members how to do things, but to give them the support that they needed logistically, and I guess you might say politically, through the military, because somebody has to open these doors. The commission, under Francis, worked very well. It was quite powerful and was well recognized, so that when we needed support of any kind, we usually got it from the military, through the medical commanders at these posts. And once the studies were under way and we were recognized at Fort Ord as being part of the military effort, it was much easier for us. But Francis was sort of the coordinator of all commission studies.

Hughes: You and the various other laboratories that were involved in these studies had full control over how the tests were to be conducted?

Lennette: Yes.

Hughes: Was there any effort to standardize the tests? Weren't there four different groups being studied across the country?

Lennette: There were several groups. Dr. Salk had one group that was studying the vaccine early on. We had one here. Other people were involved.

Hughes: There's the naval training center in...

Lennette: Yes, Great Lakes Naval Training Center. Yes, Commander John Seal was one of the early people there. Clayton Loosli at the University of Chicago Medical School had his own program and also collaborated with Seal. Joseph Beard was engaged in studies at Duke Medical School. And where else?

Hughes: Fort Leonard Wood in Missouri.

Lennette: Well, they didn't do too much there actually.

Hughes: I have Fort Dix, Great Lakes Naval Training Station, Berkeley, and Fort Leonard Wood.

#### Fort Ord Research

Lennette: Here at Berkeley we had the whole West Coast area of operations, because the army trained its recruits at Fort Ord, which was a big training center, quite different from what it is now. The number of recruits coming through there was in the thousands, and when we did influenza or adenovirus studies, we would inoculate as many as ten thousand men during the course of the season. The numbers were so large because these people were here only a matter of weeks, and then were gone, so that we had to keep continually immunizing the population. As a result, we did a lot of work, expended a lot of effort, to study an outbreak in a relatively small population. That's a large population, but relatively, in terms of the numbers of people that were immunized, it was small. But sufficiently large that we could get answers.

Hughes: Was it as a result of the flu vaccine tests, that the adenovirus problems became apparent? I mean by that, the fact that the recruits were still coming down with respiratory diseases that didn't seem to be affected by the vaccine.

Lennette: That's right. It was just like the polio thing that we mentioned. A lot of illnesses were called polio which really weren't. The same thing here--a lot of diseases were called influenza which actually weren't by laboratory tests.

From all of the people who came down ill with any respiratory disease at Fort Ord--this was also true at the other installations--specimens of blood were taken for antibody studies, and also throat washings, throat swabs, to isolate the virus. We had a large number of cases which were not influenza by laboratory examination so we knew that other agents were involved. But what were they? Well, as a result of one small outbreak, we got the coxsackie virus, so-called Coe virus. In other outbreaks later on when we knew

Lennette: about adenoviruses and were using tissue cultures for examination of throat washings, we began to isolate adenoviruses, too. So that's how we eventually recognized that the three important viral types were types 3, 4 and 7.

One of the byproducts of such studies was the finding that, number one, this adenoviral respiratory disease was peculiar to the military recruit, because you didn't see it in the counterpart age group in university populations; this group had infectious mononucleosis, which we very seldom saw in the military recruits. Also, when you got the very young pediatric age groups, the adenoviruses that were responsible for disease there were not 3, 4 and 7, but 1, 2, some 3, 5 and 6. It was a different type entirely.

Hughes: Why is that?

Lennette: I don't know why that is. The virus I guess just fits these kids, and they come down with a disease due to these agents.

Hughes: In 1957 there was the Asian flu outbreak, and I know you had a role in testing vaccines for that epidemic as well.

Lennette: Yes, we did. You see, this was one of the viruses which had a major change in antigenicity, a major mutation in the virus, so it came out to be almost a completely new agent, enough so that we had to make an entirely new and different vaccine. Stated differently, the vaccines that we used previously were not effective, because the antigenic composition of this new virus was so different.

And this is where the present day designation comes. In addition to the year and the virus, whether it's A or B, and the place of its isolation, we have a system of nomenclature which includes the hemagglutinin and the neuraminidase, and this way you can characterize the viruses. It's a whole new nomenclature which has been put forth officially by WHO here in the last few years and which is now widely used.

But there have not been very many of those changes over the years, three or four. We start out almost from scratch with a new virus. It's enough to be disconcerting. And you asked earlier about adenoviruses. Well, they don't do that. Once you get an immunotype isolated, it stays that way. Polio virus is the same way. Mumps is the same way. Influenza is rather unique. Not rather unique; it is unique.

## Adenovirus Vaccines

Hughes: I was wondering about the source of the vaccines. They were commercially made, but where did the pharmaceutical houses get the recipes initially?

Lennette: That was part of the work of the Commission on Influenza. The viruses isolated by the commission members ended up in Dr. Salk's laboratory in Michigan, and he would test the antigenicity of these various strains of virus isolated during the year by laboratories like our own. We sent him our isolates, and he would make small lots of vaccine incorporating these different strains. So he had various viruses that he would inoculate into volunteers. Then he would test the serums against the other viruses to see how much crossover there was antigenically. At the annual meeting of the Commission on Influenza, the decision was made as to which of these viruses would be used to prepare a vaccine for the next year. So this is where the manufacturers got their viral strains and used them for the production of vaccine.

This was effective because the commission as a group had the experience and the background to do this, which no small independent laboratory could do. There was no point in any small research laboratory trying to make a vaccine when you had people with that kind of expertise already available. So the biological houses made these vaccines for the commission according to its formula. And the same with the adenoviruses; they made the vaccines.

Hughes: How effective were the adenovirus vaccines?

Lennette: Very effective. As a matter of fact, once we began to vaccinate against these various immunotypes, we found that it was possible to eliminate one type, but it would be replaced by another. You immunize heavily against type 4, let's say, and you might eventually get outbreaks caused by type 7 virus. And if you immunize against 3, 4 and 7, then you get type 14 moving in, which was a common type in European recruits. So the vaccines were very effective, so much so that infection with these immunotypes could be suppressed to the point where some other immunotype moved in. Nature abhors vacuums, so if you pull something out of a population, something else may well take its place.

Hughes: Is there anything more to say about respiratory diseases in general?

Lennette: Well, we still have a number of viruses that cause respiratory disease. We haven't worked with them, because we work primarily with adult populations, but there's a very important virus of young children and infants, respiratory syncytial virus, that probably produces the highest morbidity and the highest fatality rate of any of the pediatric age viruses. It's a very important agent.

Then there are the parainfluenza viruses, which we occasionally isolate as a cause of disease in the civilian population.

Hughes: Did this lab have any particular role in research on either of those?

Lennette: No. We used to do tests for the parainfluenza, but we never found very much.

Hughes: On to polio then?

Lennette: No. [laughter] I've got one more thing that we might talk about, and that is the role of adenoviruses in tumor production. It was shown by a group in Texas that adenovirus type 12 inoculated into suckling hamsters would produce tumors. In other words, it's oncogenic.

Following that observation, a number of other adenoviruses was shown also to be oncogenic in animals. But so far as man is concerned, I don't think there's ever been any good evidence that these viruses produce tumors in man. Nevertheless, the experience is such that one hesitates to use these agents because of the potential for oncogenicity.

We never felt that there was any great hazard to this, because you're dealing with a different animal species and you're dealing with a different age factor. In other words, a young hamster is much more susceptible to this than an older hamster. That's also true of man. You know, the younger the animal, the more susceptible it is. But there was enough concern that any vaccine containing these strains oncogenic for hamsters would not be approved for use in man.

Well, the other approach then was to inactivate the adenovirus vaccine with formaldehyde. However, this did not produce a very good vaccine when you did that, and you still had those objections about inoculating material which might not be completely inactivated.

Lennette: The best way to immunize our military population would be to give the live virus on the presumption that the virus gets down into the gut, multiplies there, and colonizes the intestinal tract. So how is this going to be different from what you can do by artificial means? This is an abnormal route of infection for a respiratory virus. So we put the virus up in enteric-coated capsules which will dissolve in the bowel, and thus colonize the gut with a virus which will infect and produce immunity. This has been done. It has been done in the military establishment. There have never been any untoward effects. None of the data that were derived from long-term follow-ups show that there is any oncogenicity, so the vaccine has been used with very good effect.

That's probably the way we should go, but adenoviruses of the serotypes used by us don't seem to be much of a problem in the adult civilian population. It's mostly the military population.

#### Poliomyelitis

Lennette: Now we can go to polio. [laughter]

Hughes: I wonder if we could first start with a more general question, namely the role of tissue culture as improved or developed by Enders, Weller, and Robbins in 1949.\* It so happened, as you know, that they were working with polio virus, but the technique of course eventually was much more widely used than just with polio virus. What they did was to grow polio virus in non-neural tissue. Could you say something about the impact of that achievement on viral research?

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\*J. H. Enders, T. H. Weller, and F. C. Robbins. "Cultivation of the Lansing strain of poliomyelitis virus in cultures of various human embryonic tissues." Science 109 (1949):85-87.

## Early Polio Vaccines

Lennette: On one of these occasions I mentioned the difficulty of making a vaccine against polio. That was because the only experimental host we had in which we could passage the virus at that time (this is in the late forties) was the rhesus monkey, which was the animal that most investigators used. For research purposes, you had to inoculate monkeys either intranasally or intracerebrally, following which they would develop poliomyelitis. As the name implies, poliomyelitis is an inflammation of the grey matter of the spinal cord, and that's where you would find the virus. Thus, the only source of virus then was the spinal cord, which was removed from a paralyzed or moribund monkey, stored in glycerin, and then you could pass the virus by injecting spinal cord ground up in a mortar into a suspension.

If you tried to make a vaccine out of such material, ground it all up and added a diluent, say saline or Ringer's solution or whatever, you could make a suspension which was pretty turbid. Even after you attempted to centrifuge everything out, it was still fairly turbid. And if you inactivated that and tried to use it as a vaccine, you ran into trouble. Maurice Brodie in New York made such a vaccine, and although it was inactivated with formaldehyde and apparently seemed to be a good vaccine in so far as tests in monkeys were concerned, it did produce some cases of poliomyelitis in people who were given the vaccine.

Another attempt along this line was the Kolmer vaccine. This was the [John] Kolmer who devised the Kolmer test for syphilis. He was in Philadelphia, at the University of Pennsylvania, and made a vaccine using the same sort of procedure, except instead of formaldehyde he used sodium ricinoleate to inactivate the polio virus in the spinal cord suspension. Here again, there was a number of cases of poliomyelitis consequent upon administration of the vaccine. So people pretty much gave up on attempting to produce a vaccine this way. The starting material was not only crude, but the neurologic tissue content could conceivably be harmful on repeated inoculation.

Such material didn't make a very good antigen for laboratory serologic tests either. It was pretty crude, had a lot of goop in it that was nonspecific and interfered, so that there was no way to test it except, again, by the so-called neutralization test, using monkeys. It's catch-22; monkeys were expensive, and it took a lot of them to do a viral titration. We always felt there ought to be a better way to do it.

## Tissue Culture

Lennette: Enders and Weller and Robbins in 1949 ushered in the tissue culture era in virology. Cell biology about that time was getting a pretty good start, and we were learning how to grow cells in various kinds of media. Now Enders et al. gave us the ability to grow cells and viruses in media which were quite clear. The best medium was 199, which is the number of the formula for the fluid component; we won't go into how that was derived, because that would be a long story, too. But medium 199 was the liquid part, and the tissue cells themselves originally were human foreskin tissue, and then later on, rhesus kidney. The Enders group was able to show through the use of non-neural tissue that you could cultivate the cells and get them to grow, and that, after the cells had grown out, if you inoculated them with polio virus, the virus would multiply.

This was a tremendous breakthrough, because here you had a simple, in vitro technique. If you used the two kidneys from a monkey, as I believe we mentioned on one occasion here, and employed a technique that was developed to separate the cells by breaking down the binding matrix, the collagen, by trypsinization, and then washed the cells, you could get a working suspension containing millions of cells. Then, if you counted the cells, and, say that you used fifty thousand cells as a basis for making a tube culture, you'd have enough cells in these two kidneys to produce anywhere from fifteen hundred to two thousand culture tubes, each culture tube now being the equivalent of a monkey. As you see, you could do a tremendous amount of work with such a tissue culture system. You could produce a lot of virus, and if each tube represented one monkey, then you could do all sorts of titrations never feasible on such a scale before.

This opened up a whole new area of poliomyelitis research, because you could not only do epidemiological studies, but you could make accurate diagnoses, and you could also produce large amounts of virus.

Using such materials, Nathalie Schmidt and I were able to devise the complement fixation test, which was simpler than trying to do neutralization tests, although it eventually came out that the neutralization test was a much better test. And then this was simplified into the metabolic inhibition test, which used wells in a clear plastic plate rather than tubes. These were great advances, no question about that.

Hughes: Did you introduce tissue culture into the lab very quickly?

Lennette: Yes. That was part of our job, all these new techniques that came along, to put them into the laboratory as promptly as possible. I sent one of my staff, Anna Weiner, to spend some weeks in Boston with Drs. Enders and Weller and Robbins. She came back with all sorts of information and started the tissue culture work in this laboratory. Taught some of the other people. And then by extension, the rest of the staff learned it.

Hughes: Do you remember when she went?

Lennette: It was right after the cultivation of the polio virus was described. It was either late '48 or very early '49.

Hughes: What about equipment? Did the supply houses immediately get on the bandwagon?

Lennette: Enders et al. had shown that the best way to grow these cells in a tube was to put them into a device called a roller drum. The drum consisted of a double plate, with perforations to hold fifty or so tubes at a slight angle. As the drum revolved, with the tubes nearly horizontal, the medium would wash over the cells, so that they were always being alternately immersed and exposed to air.

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By this procedure, the cells would produce a great deal of virus. Of course, you had to grow the cells out first, and then after you had a nice monolayer of cells which you inoculated with polio virus--or any other virus that you happened to be studying--and the virus would grow very nicely in this cell system.

Well, these roller drums were newly introduced commercially, and while they were expensive, they had cheap motors in them, which would break down for no obvious reason. To get around this, test tube racks were devised, made of stainless steel, so that you could put the tubes in at an angle; there was a little clip that kept the tube from falling out. Since they were inserted at an angle, you could keep these racks stationary and you could stack them up one on top of the other because they had little flanges--the top had a flange which fit into the bottom of the other so you could stack them up. And for many viruses, this system worked perfectly all right--we didn't have to use the roller tubes. These were all advances. This was very helpful for doing neutralization tests, also.

However, when the microprocedures came along, the metabolic inhibition test using clear plastic plates, you could do large numbers of tests without buying a whole warehouse full of incubators. The plastic plates were relatively thin, had wells in

Lennette: them, and could be stacked one on top of the other, so that you had a pretty good number of plates in any one incubator. These were all developments that came quickly over several years. And of course people were applying these techniques to other viruses, too, so that a whole new era of virology opened up. Usually in cases like this, you don't have much difficulty in getting biological houses or supply houses to make equipment for you. If you have an idea something is going to work, and if you can interest the representatives, they'll make the equipment for you and let you try it out.

Hughes: Of course in this case the technique had implications beyond virology, in other basic sciences.

Lennette: Sure. Well, these people see a market; they help you develop something; they're the firstest with the mostest. They've got a real stake in it.

#### Polio Research at the Virus Laboratory

Hughes: Tell me how this lab became involved in polio research.

Lennette: As I think I mentioned, it was not my idea to work on polio again. We were pretty well occupied doing field work and laboratory work on Q fever. We were interested in the rickettsial diseases, and this was about all we could handle in the laboratory from the standpoint of space. We didn't have any place to house all the people added to work on polio. We were also doing some work at that time on the respiratory diseases, primarily influenza, and we were also running a diagnostic laboratory. We were pretty well committed from the standpoint of space and staff. I didn't need any more headaches, like poliomyelitis.

Now mind you, I was familiar with the polio field because my Ph.D. degree in microbiology was earned on the basis of the research work I did on polio at the University of Chicago. So I knew what the problems were in that field of medicine.

When we were asked by the National Foundation for Infantile Paralysis to set up a diagnostic laboratory for the eleven western states so we could tell during the vaccine field trials whether patients who had been vaccinated were coming down with polio or some other disease mimicking polio, I wasn't too keen on that. I pointed out we didn't have the room, and when I had asked for some additional space previously from Dr. Halvorson, the director of the department, he couldn't find any. This is early fifties.

Hughes: So this was earlier than the Salk vaccine trials?

Lennette: Yes, the trials began in about '54, around in there somewhere. The Acton Street laboratory had been going for some years. When I came and we got all these other diagnostic tests going, we were pretty well occupied with the things that we had to do, and we didn't have very much space to expand. So I used that as kind of a weapon. Where are we going to go? There's no space here. We wanted space for other things, but not for polio.

Let's go back just a moment. Prior to the Salk vaccine, it was shown that gamma globulin had a protective effect, so if you used human gamma globulin, you could use it prophylactically in the face of an outbreak of poliomyelitis and confer protection.

I had been asked to head up that study. Henry Kumm came out here to Berkeley. He was an old acquaintance, a former colleague in the Rockefeller Foundation who had run the yellow fever laboratory at Bogota, Colombia, for some years. So since we had both worked on yellow fever--I was in Brazil at the time--we had something in common. Henry came out to see if he could persuade me to take on the field trial. I guess I wanted everything, including the gold-plated sink. Which they weren't about to give me. And I wasn't too interested. I could see a lot of headaches in a field trial of that magnitude.

So Dr. William McDowell Hammon at the University of Pittsburgh took on the task of assessing the value of gamma globulin. He was an old friend, too, because he was professor of epidemiology across the street here at the U.C. School of Public Health before he went to Pittsburgh. He did the study, and showed that gamma globulin was very effective, and the national foundation was all ready to go and use this as a prophylactic tool in polio outbreaks.

Hughes: This was early fifties?

Lennette: Yes, this was the early fifties. At that time our headquarters--we were still a small department--was in San Francisco in the Phelan Building. Mr. O'Connor himself came out to meet with department staff to see if we would take on distribution of gamma globulin statewide whenever outbreaks occurred. I was opposed to it, as were many other people, too, because there just wouldn't be enough gamma globulin in the country.

At one stage I was sitting fairly close to the end of the table. Mr. O'Connor was next to me. I asked him why they wanted to foist this bastard child on the California State Health Department when they knew there wouldn't be enough gamma globulin, and that the national foundation would retire with all the satisfaction and all of the kudos for having shown that this was

Lennette: a very effective procedure to prevent polio, but we and the poor health officers in all these counties would be getting all the flak for being unable to get gamma globulin. As far as I was concerned, this was for the birds, and I wouldn't have any part of it. Now mind you, I was not the health officer. It was not for me to say what would be done in the state or not. So that sort of terminated that meeting. [laughter]

Dr. Halvorson, who was the director of public health, I think sort of blanched a bit, and then he colored a little bit. This was on a Friday afternoon. So I went home thinking that the telephone is going to ring on Monday morning and tell me that my appointment with the department was now severed.

Well, I did get a phone call, but it wasn't that I was fired. It was to the effect that the availability of funds for poliomyelitis research would be limited, and that any position such as I took certainly didn't speak well for my getting any national foundation money to support polio research. Well, I wasn't too concerned about that, because I didn't want to do any polio research anyway, except that the foundation, and very rightly so--they had a great deal of perspicacity--was supporting research on other viruses, such as St. Louis and western equine, which would give them models for polio. So we had sort of a tiff there. Well, that showed my position on the polio problem.

Then when Mr. O'Connor, through Dr. Kumm, wanted this laboratory to be set up as the reference laboratory for the eleven western states, I didn't want to get involved because that would really be a tremendous effort.

#### The Salk Vaccine Field Trials

Hughes: This is in connection with the Salk trials?

Lennette: This is with the Salk trial, yes, because the vaccine came along shortly thereafter. We had to know whether we were producing polio with the vaccine, or whether people were not totally immunized and getting polio from wild virus, and so on. So I used this as an excuse to Dr. Halvorson. I said, "Well we can't do it. We just don't have enough lab space here." Up to this point we had an industrial engineering laboratory around the corner from us, on Acton Street. Well, it was part of the same land plot, although it faced on Acton Street. We faced on University Avenue. What had been done to give us a little bit of additional space, between '46 when I left and when I came back in '47, the corner plot had been filled in with more lab space. Part of that was for the Virus Laboratory, and a piece of it was for Industrial Hygiene. We had sort of an L-shaped building. And we couldn't get any more space. It was just impossible.

Lennette: Then when Mr. O'Connor came along and wanted the Virus Lab set up to do this project, the chief thought this was in the public interest, it ought to be done, and that we were in the best position to do it, so why don't we go ahead. I said, "We just don't have the space, chief." Within a week we had the space. Everybody else got moved out. He said, "Here it is." Out of that we got that whole Acton Street site. And that's how we got involved in polio. It was a good experience, and we gained a lot of knowledge on poliomyelitis and on the vaccine and so on.

Hughes: How were the field trials set up?

Lennette: First it was on the clinical side. Salk tested his vaccine in small groups of children to be sure that it produced antibodies. Then he had some data that indicated when outbreaks came along, these children would be protected. From that small trial they went into larger groups. Thousands of children were to be inoculated, and if they came down with some kind of illness or disease, then we wanted to know if that was nonparalytic polio or paralytic disease due to the vaccine or to some other agent. Of course, we weren't too knowledgeable about it at that time. It was only later on that we showed other viruses can produce transitory paralyzes which look like polio.

That was our job, to sort out the illnesses--and being a diagnostic laboratory, we had a unique capability to do the sorting. This was done on a massive scale. We used five thousand tubes or so of cell cultures a week which after sterilization were taken down to the Bayshore to the dump and disposed of. I'm sure that about a hundred years from now when somebody digs in that midden and finds all these plastic tubes, and glass tubes too, for that matter, they're going to wonder what kind of a civilization existed here in Berkeley.

But that's about the time that the test was brought down to miniature size in the plates. This again is another example of being unable to pursue a problem, here an in vitro neutralization test, because the technological underpinning was lacking.\* Thus, C. H. Huang, a Chinese student working with Claus Jungeblut at

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\*Dr. Lennette added the following explanation after the interviewing process had been completed.

Lennette: Columbia University College of Physicians and Surgeons in the mid-thirties showed that a virus growing in tissue cultures would kill the cells. Since dead cells do not metabolize, the phenol red indicator dye he used would not change color because no acid was produced. If, however, a serum containing antibodies specific for the virus were added, the virus would be neutralized, the cells would flourish, producing acid, which would turn the indicator dye from magenta to yellow. This was the essence of Huang's system, but neither he nor we could make practical use of it because of inability to quantitate the cellular component. Remember, we were using the rather primitive Maitland-type cultures comprised of minced chick embryo tissue. It was not until the late forties that quantitation became possible when Enders and his associates used trypsin to break down the matrix binding cells together, thus making it feasible to count cells in suspension and employ whatever numbers were desired in an experiment, that is, standardization was attainable. This permitted standardized procedures for conducting neutralization tests, first in tubes and later by a micro method employing plastic plates with as many as ninety-six concave wells, which permitted titration of antibody using standard numbers of cells and standard, predetermined amounts of virus. Over the years, since Salk first worked out this technique, there has been virtually no change in the method.

Hughes: I understand that polio was tricky to work with, that the pattern of excretion, for example, of the virus is very intermittent, and you discovered in the process of these trials that it was not quite so straightforward as it first appeared.

Lennette: Yes, this laboratory had some very good data on that. Showed that excretion of virus does fluctuate.

Hughes: So again, was it a question of continually updating the physicians in the field who were sending in the specimens?

Lennette: No, that was pretty well established that we should get the laboratory specimens from patients as early as possible. Sometimes they would send in two or three, because the patient would be hospitalized and they would...

[telephone interruption]

Hughes: We were talking about potential problems with informing or updating physicians in the field.

Lennette: Well, there was so much publicity during the course of these trials, about how they were going and how many people had been examined and how large the morbidity was and so on, I think everybody was pretty well aware of developments, especially the pediatricians, who have always been interested in infectious disease. They sort of carried the ball. As far as updating is concerned, once the disease began to disappear, I think people lost interest in it.

Lennette: That certainly is true today. A lot of these young doctors have never seen a case of paralytic polio. They know nothing about hallways filled with respirators. They just don't know the disease. Just as many students have never seen a case of smallpox in this country. I never saw any smallpox when I was in medical school. It wasn't until I worked in the tropics that I saw cases of smallpox, actually variola minor.

So here again, once the emphasis on vaccination was over, the general public sort of lost interest in it. "The disease is under control."

Hughes: What about Tommy Francis' role in the Salk trials?

Lennette: Francis was a very good clinician on respiratory disease. His training at Yale and at the Rockefeller Institute was primarily clinical, although he had worked in the laboratory, and he was also a very good epidemiologist. About 1937 or 1938 he became head of the epidemiology department at the University of Michigan School of Public Health. He was one of the outstanding top level scientists in the country, and seemed like a logical choice to head up this study group. Gordon Brown at Michigan was working on polio at the time, so that they had some staff members who knew quite a bit about the laboratory side of it. As Tommy was such an outstanding epidemiologist, why not get him to set up a group to study the efficacy and safety of the vaccine.

First, he set up an advisory committee, of which I was a member. It was this committee which laid the plans, but mostly the massive field trial was a reflection of Tommy Francis' own wisdom. It was also based on our past experience with influenza vaccine field trials in the military under the auspices of the Commission on Influenza of the Armed Forces Epidemiological Board.

So he set up this polio vaccine field trial and decided how the patient specimens ought to be obtained--not the details, the nitty gritty, but principles. Somebody receives a vaccine shipment to test and he comes to you, "What do we need? Where do we ship it? How do we ship it?" This sort of thing. Tommy worked out the machinery for it, which was implemented by the national foundation people. It worked very well. So that was his contribution. And it was a tremendous job well done.

After all the field trials had been done, they had a big meeting at Ann Arbor, which I was unable to attend, although I was a member of the advisory committee. At that meeting the stamp of approval was given to the use of the vaccine. It was

Lennette: premature in view of what happened subsequently; cases of poliomyelitis appeared postinoculation. Well, there are a number of reasons for that. But in any case, the vaccine was approved for use in man. It was widely distributed and used, and then we had cases of polio occurring.

One of the difficulties lay with Cutter Laboratories. Not that the problem was anything unique, but Cutter was a latecomer to the scene. They were producing polio vaccine according to the protocol laid down by the Bureau of Biologics, at that time a unit of the National Institutes of Health, but transferred to the Food and Drug Administration as an aftermath of the "Cutter episode."

The vaccine had been approved, prematurely I think. Here was a vaccine which had the stamp of approval by the NIH, so let's go and manufacture it and begin the inoculation campaigns.

Hughes: By what criteria did you judge it to be premature?

Lennette: Well, premature in the sense that there was a lot of political pressure applied. "See, we've got a vaccine now. Let's get this ball rolling." Now I'm talking in retrospect, and I'm also talking post facto. I was not at the wrap-up meeting at Ann Arbor, but the repercussions--or at least the information I got over the grapevine--indicated to me that there was pressure exercised to approve the vaccine. There was unease in some quarters, but a lot of the objections were either ignored or overruled.

Hughes: And there were several objections from rather prominent individuals.

Lennette: There were.

Hughes: Enders being one, and Karl Meyer being another.

Lennette: And I was, too, because I raised some objections at one of these meetings of the National Institutes of Health. John Enders and I were a minority of two at that meeting, so far as I know, and neither of us was invited back again.

Hughes: What were you arguing?

Lennette: Well, we didn't feel that the vaccine safety had been that firmly proved.

Hughes: You felt the preliminary trials should continue?

Lennette: No. This was after several cases of polio had occurred and we felt the whole process of inactivating the virus should be reexamined and reevaluated. During the Ann Arbor meeting, pressure had been brought to bear to officially approve the vaccine for manufacture and release despite grave reservations by some scientists.

A reflection of some of this unease occurred during a prevaccine trial meeting in New York City at the Commodore Hotel in 1953 or 1954, before the large scale field evaluations of the vaccine were initiated. Tom Rivers was there, Tommy Francis, Joe Smadel, and Colin MacLeod, all of whom were deeply involved. These were people to whom you might apply the term "the establishment," not in a pejorative sense, but in recognition that these were the elder statesmen who knew what the polio vaccine trials were about. These were the "old graybeards" who had been through the mill of medical science and knew what it was all about.

The question was raised as to whether the vaccine would be safe at the present level of inactivation with formaldehyde. And I remember distinctly Tom Rivers saying, "If you put any more formaldehyde in, you'll make it so damn safe it won't be any good." That's recorded somewhere in the minutes of that meeting.

Hughes: Was it experience that he was basing that statement on?

Lennette: No, what might be called "phase one" clinical tests had been done in man; extensive tests had been done in monkeys, and nothing had happened. Nevertheless, there was still a certain amount of intuitive unease as to whether, as you accumulated numbers, safety would stand up. Theoretically it should. But there was some unease. And so the formula was kept the way it was; no changes were made. And I remember Colin MacLeod raising the question whether this was really the way to go, but that's the way the matter stood, namely, "We'll go ahead and make the vaccine." Well, the vaccine was made that way. Then Cutter made several batches of the vaccine, which upon inoculation into man produced cases of poliomyelitis, some of them with severe paralysis.

There thus arose two camps of opinion as to the cause or the basis for this tragedy.\* On one side was Jonas Salk, who never admitted that the virus inactivation method was at fault. On the other side were those who insisted that the basic premise

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\*Dr. Lennette added the following four paragraphs after the interview process had been completed.

Lennette: on which the inactivation curve was based was erroneous and misleading. Based on experimental data, an inactivation curve was plotted with viral concentration as the ordinate, and time, in hours or days, as the abscissa. The curve was essentially a straight line, the virus titer falling linearly as a function of time to the point where infectivity was practically undetectable. This is where the curve approached the base line, and the Salk group merely continued the curve below the baseline. This extension represented the time required to completely inactivate the virus.

Others--Wendell Stanley, Sven Gard, Enders, Herdis von Magnus and myself among others--disagreed, convinced that the inactivation process did not follow a straight line and it was not permissible to extend the curve below the baseline. The curve, rather than being a true line, became asymptotic, that is, as the amount of infectious virus became infinitesimal, the curve tended to run a course parallel to the base line. In other words, unless due precaution were taken, some infective viral particles would survive the inactivation process.

Hughes: Why were you in that camp? What was your basis for saying that?

Lennette: First, because cases of poliomyelitis occurred in vaccine recipients, and second, live virus was found in the incriminated lots. In addition, the Mahoney Type 1 strain was a poor choice to include in the vaccine. This is because the Mahoney strain was sort of capricious in that there was a very small margin between complete destruction of infectivity and the ability to produce antibody.

Hughes: Was it Salk who had chosen that strain?

Lennette: Yes.

Hughes: What were his reasons?

Lennette: Well, he thought it was a good strain. People have reasons of their own. They're not always obvious. So he used that strain.

Hughes: And I believe the British used another strain when they came to produce their own inactivated vaccine.

Lennette: Oh yes.

Well, to get back to Cutter. Cutter was producing the vaccine according to the formulation put together by the committee--well, Salk really laid down the basic procedure, how much formaldehyde to use, how long to incubate and how and when

Lennette: to test for the presence of residual live virus. You had to inoculate so many monkeys, and then these monkeys had to be killed and the spinal cords examined by pathologists well versed in poliomyelitis pathology. Every possible approach was used to be sure the virus was inactivated and there was no live virus left.

Well, if you produce vaccine on a small scale in the laboratory, that's one thing. You start to produce it in massive amounts, in liters and liters, that's something else. The genetic engineering business today has definite restrictions and guidelines. You can produce a product in the laboratory and all goes well if you work with less than ten liters. If you want to go beyond ten liters, then you've got all kinds of problems with the authorities because of possible hazards, so you have to get special permission and whatnot. So here, too, when they began to make the vaccine, some of the manufacturers who had been making it all through these several years of the field trials knew that occasionally they would get a bad batch, and they would just inactivate it some more.

Now along comes a new manufacturer like Cutter or whoever, because they were not the only ones, and faithfully follows the cookbook procedure, which is laid out by the federal authorities. The tests as they do them in the laboratory showed there was no virus in the vaccine, and yet when it was inoculated into man there was a problem of infectivity. You should take a second look at the method and see what's going on. The obvious conclusion is that the technique is inadequate.

Hughes: Why was Cutter one of the labs chosen? It was the only one, I believe, that hadn't had previous experience in producing vaccine.

Lennette: At that time it was a big pharmaceutical house on the West Coast. They needed people to produce the vaccine.

Hughes: And there wasn't anybody else?

Lennette: There were several other people. Parke-Davis produced vaccine, as did Merck.

Hughes: I mean here on the West Coast there was no other choice.

Lennette: No, that was the largest pharmaceutical house on the West Coast. And they had produced other vaccines, for distemper, rabies, or whatever.

Hughes: The virus itself was grown in Canada at the Connaught Labs. What is the story behind that?

Lennette: I don't know what was behind the choice of Connaught up in Canada, but they were making the Salk vaccine for Canada. Connaught Laboratories was very closely tied in with the University of Toronto.

Hughes: And the university was doing some polio work?

Lennette: No, but they've always collaborated very closely. So when the Canadian vaccine was to be made, they just chose Connaught. They made the flu vaccine at the Connaught Laboratory. It was a big manufacturing plant. They made the polio vaccine.

The Cutter Laboratories dropped out of the program. Then other cases of poliomyelitis occurred which were blamed on the vaccine with no good evidence that it was the vaccine. So other manufacturers became pretty disenchanted, and over the years they have all dropped out. I think Merck is the only one that's left to produce vaccine in this country. Well, this includes also live vaccine.

See, when the live vaccine came along, most people in this country began to use the Sabin live polio vaccine, and manufacture of killed vaccine in this country ceased. I don't know of anybody who made it. So if you wanted it, you had to get it from Connaught Laboratories. And then you had to go through all the importation, customs, and whatever, to get it cleared. So a physician himself wouldn't want to get the vaccine unless he had a big practice and could get it through his distributor.

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National Drug Company had a unit near Philadelphia devoted to vaccine production. What with the greed and rapacity of liability lawyers, National decided to give up manufacture of all vaccines, not just polio, just gave their plant to the Salk Institute to use for production of whatever they wanted in bulk. The Salk Institute didn't have all that kind of use for it, so they leased it to Connaught Laboratories, who are now producing Salk-type vaccine.

Hughes: Two weeks after the trials were begun, there of course was the Cutter incident, and the Surgeon General stopped any further progress on the trials.

Lennette: Well actually, it was the State of California that really stopped the use of Salk vaccine.

Hughes: Would you explain that?

Lennette: Well, when we had the first cases, Cutter telephoned the California Department of Public Health to let them know that several people had received Cutter vaccine--they had the lot numbers and everything, because it was part of the record keeping--and had come down with polio. We were notified, and as a matter of fact, we had done tests on some of these patients. It was obviously polio.

Hughes: This was right away?

Lennette: Yes, it was just the first batches being released. And Cutter all through this acted with responsibility. They weren't trying to hide anything. They were very responsible in their actions, and they gave every support possible. So then the question arose, what do we do here in California? We're using a vaccine. We've got I don't know how many cases of poliomyelitis.

So one evening the director of the Department of Public Health in California, Malcolm Merrill, Robert Dyar, A. C. Hollister--Dyar was director of the Division of Research in the department; Hollister was chief of Infectious Diseases--and I, a laboratory person and epidemiologist, met in Dyar's home to discuss this problem. We had dinner there, and then sat around all evening talking, considering, and debating, with the result that at about two or three a.m. eastern time we called the office of the U.S. Surgeon General and told them what had happened, and that we were planning to stop vaccination. We also called the Bureau of Biologics people and told them we had these cases of poliomyelitis, and that vaccination in California would be stopped, effective immediately.

Hughes: How many cases did you have?

Lennette: Oh, I don't know how many we had. It was enough to shake us. It must have been half a dozen or so at that stage. This was the first blow out of the box. We didn't know what else was coming, but the mere fact that we had cases of poliomyelitis following inoculation of the vaccine within a few days was enough to give us pause. So we decided to stop the immunization program.

Well, what happened was the Surgeon General's Office released the information to the press--all vaccination was being stopped nationwide. They actually had known nothing about this until we told them, so factually it was the director of public health in California who administratively stopped the vaccination program. Not that the Surgeon General was trying to preempt whatever it was, but that's the way the press put it together, you see.

Hughes: Of course. Very shortly after the trials were stopped, the Surgeon General, who was Leonard Scheele, called a meeting of scientific experts in Washington, I suppose it was, April 29th and 30th, 1955, at which you and...

Lennette: John Enders.

Hughes: ...and many others were present. Could you describe what you discussed at that meeting?

Lennette: Well, as usual at this kind of a meeting, what happened was a great deal of discussion and a lot of detail. Of course, everybody is pointing out what happened in his experience and what he thinks. And eventually after a day or a day and a half, you really shake things down; you get down to the nub of the problem and you make a decision.

And the decision was that there ought to be revamping of the manufacturing protocol. The protocol for the production, manufacture, whatever you want to call it, of the poliomyelitis vaccine was not adequate. There was something amiss with the inactivation procedure, so that we should take another look at this and get into the act and see how much more formaldehyde we should add and how much more...

Hughes: Now was that pointing a finger at Salk?

Lennette: Not necessarily, because he was the one who came out first with a lot of the data, but there were other people involved. This was sort of a group effort. Experience of groups was pooled. This wasn't something that Salk himself put together and said, "Here it is, folks, this is the way you're going to make the vaccine or else." No, it never came to that. Salk was open-minded in that respect, and he had input from others.

But the final protocol that came out to make the vaccine just was inadequate from the standpoint of safety. They did finally come up with some new recommendations--and this involved the people at the Bureau of Biologics, who had a great deal of experience because of their examining process. They went into all of these manufacturers--they do this all the time--to see how the vaccine was being made.

When the new, revised procedure for killing the virus was adopted--I don't know all the changes, and especially the major ones, that were instituted--the vaccine was all right.\* Doubts as to the real safety of the vaccine persisted in some quarters,

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\*Dr. Lennette added the following paragraph during the editing process.

Lennette: but the trials were resumed slowly and cautiously, and these fears were resolved. Following the occurrence of postinoculation poliomyelitis among the original group of vaccinees, Francis and his staff at the Vaccine Evaluation Center in Ann Arbor went over all the mass of data from the population inoculated in the early trials, and from these clinical, epidemiological, and laboratory findings came to the conclusion that some mild and subclinical cases of polio had occurred but were not detected.

What this does is two things. It shows the unease, the uncertainty with some of the people as to whether the vaccine was really safe to administer. Well, after it was all over, when Francis and some of the other epidemiologists went over all of the data clinically and epidemiologically, they came to the conclusion, yes, some of these cases well might have been poliomyelitis that we missed. Just minor cases.

Hughes: When were the vaccinations resumed?

Lennette: It wasn't too long. It was just a matter of a few months.

Hughes: Using a more stringent inactivation procedure, I'm sure.

Lennette: Yes.

Hughes: Would you like to comment on the legal trials that followed?

Lennette: Those trials which came up in the instance of people who had received the vaccine and then some days later developed poliomyelitis, I think that was fairly clear cut as to cause and effect, the association of paralysis with the injection of the vaccine. It was only later--and this was concerned primarily with the Sabin vaccine, which is a live virus vaccine--that things got a little bit out of line.

The Sabin vaccine used three different virus strains, types 1, 2 and 3, which genetically were avirulent, and on the whole did nothing in man, at least nothing in children. But occasionally an adult would come down with poliomyelitis, maybe one person in five million.

Well, we didn't have any really good markers that would distinguish a wild virus as it occurs in nature from a laboratory passaged, attenuated virus, such as the strains in the vaccine. It's the same old story--the insurance company has got plenty of money, let's give it to this poor child or this poor woman or whoever had polio, not paying necessarily a great deal of attention to the factual situation. So in some cases where a

Lennette: laboratory, and especially the Center for Disease Control, could show that the virus that was recovered from the stools of this patient was a wild virus, not a vaccine virus, this didn't always influence the jury. It was perhaps too esoteric. Juries are easily swayed by anybody, I guess, who is a suave speaker and very emphatic about his opinions. I've seen this happen in study sections. One person can change the opinion of eleven others.

There was one instance in Texas where it was decided that the individual was paralyzed after the vaccine, and somebody ought to be responsible and have to pay for this, so let the manufacturer pick up the tab. That was a pretty big tab, several million dollars. You want justice, you don't want people being held responsible when the data aren't there.

That kind of situation is the sort that puts people out of business. So many lawsuits have been settled by juries which gave not only what was asked for, but sometimes even more money. Many of the manufacturers got out of producing the vaccine. There's only one left now, and that's Merck. And I don't know how long Merck will continue to make it. All they need is one or two more lawsuits, because biologicals aren't all that profitable.

Hughes: How did Cutter survive?

Lennette: The insurance picked up a lot of it. But that was a pretty bad situation, too. Most of the manufacturers are insured, but sometimes the decisions are made on a basis which is unfair, and if you get people into court who produce a lot of data with esoteric tests, it's hard to convince a jury.

Of course, making vaccines should be a lot easier now since the advent of the recombinant DNA techniques. We can do homologies. We can, for example, follow some viruses right through a population, their footmarks are so obvious and so characteristic. If we use recombinant DNA techniques-- methods are going to be developed for diagnostic labs; that's a coming procedure-- it'll be possible to say this is a wild virus or it isn't without any question. It's not going to be subjective. It's going to be objective and certain.

## The Sabin Vaccine

- Hughes: Well, let's talk about the live polio vaccine. Your friend of yellow fever days, Hilary Koprowski, I understand developed a live polio vaccine early in the fifties and tested it, I believe, in New York, and also at Sonoma State Hospital. Did you have any association with any of that?
- Lennette: He and Herald Cox--Herald Cox was the director of research for Lederle Labs at Pearl River, New York--were working on attenuated polio viruses, to the point where they had several of them. One of them was the so-called Fox strain, named after John Fox, and the other one--the name escapes me. They used these to make vaccines. But I think the problem there was a personal one, in part--dissension between Koprowski and Herald Cox over which way to go on this. And the other was that Albert Sabin, I guess, was going much faster.
- Hughes: Was that because he had more money?
- Lennette: Well, support. Plus how to do things. They had different techniques, I suppose. I don't recall all the details of Koprowski's work.
- Hughes: Do you know anything about the stand of the National Foundation for Infantile Paralysis? At some point there must have been a decision to go with the Salk vaccine as opposed to the Sabin vaccine. Was that an easy decision?
- Lennette: Well, I think that was an easy decision to make, because Salk was the first one on the scene. He had a good vaccine which was producing antibody. And he himself had said that the vaccine perhaps would not be entirely protective, but if there's any wild polio virus in the community, the vaccinated person will pick some up, it won't produce disease in him, but it will reinforce his immunity.

So you've got a vaccine in which the virus is killed. It's been tried in thousands and hundreds of thousands of people, and that's the way to go. And why look for another vaccine? So all the money was being poured... Well, for live vaccine, Lederle was using its own money to develop this vaccine. It was commercial.

Salk was the national hero, or international, too, I guess, so that he had all sorts of support. You might say that the money for support of Salk's research came off the top of these money drives for the national foundation.

Lennette: Sabin felt, as many scientists did, that the best way to immunize against any disease is to use the live agent, bacterial or otherwise. So why not use an attenuated polio virus for this purpose? You would get a solid immunity, just as you would if you were actually infected. The national foundation wasn't willing to support him. So for a span of a couple of years, I guess, he didn't get any support except incidental from other sources.

Hughes: Why was that?

Lennette: A lot of it is personality, too. Well, you didn't know Mr. O'Connor, but he was a very forceful, aggressive New York lawyer and he pretty much ran the national foundation with a high hand, like a private fiefdom. What he decided to do generally was done. And if he didn't like what some of his committees were doing, he would dissolve them and reassemble a new one.

Hughes: Why was he so much in favor of the Salk?

Lennette: Two things. He was ill, I understand, and he wanted to see poliomyelitis vanquished in his time. Which occurred. You can't take that away from him. He singlehandedly saw what could be done and pushed hard to get it. From the standpoint of picking the right person at the right time and giving him all the support he needed, namely Salk, I think he did the right thing. And it paid off. He did see polio conquered in his time. If any more was to be done, he felt probably that Salk would be the person to do it. He thought we don't need a live vaccine. Now I'm just guessing. I don't know because I didn't talk to him. I always discussed these matters with Albert Sabin.

Sabin felt that he had been shortchanged by the foundation, that they never gave him a fair shake. I spent all one evening in the bar of the St. Francis Hotel in San Francisco discussing these things until the small hours of the morning, and he was a pretty bitter person about the lack of support, and, in my judgment, justifiably so.

Hughes: This was before..?

Lennette: This was after the Salk vaccine and before the live vaccine trials began.

So how did he get his supportive data? He had to go outside the country. He did a lot of his field trials over in the Soviet Union. Couldn't do them here; he had no support. But the Soviet Union gave him the support he needed. People like [Mikhail]

- Lennette: Chumakov, who was the director of the Institute for Poliomyelitis and Encephalitidies, made vaccine according to Sabin's formulation using his strains, and they tested it in the Soviet Union, and showed that it was effective.
- Hughes: Did the Soviets make the decision in favor of the Sabin vaccine because live vaccines in general are more effective?
- Lennette: It's a matter of philosophy. Many of the scientific leaders firmly believed the live virus vaccines--polio, influenza--were the way to go.
- Hughes: It didn't have anything to do with the politics that were going on in this country?
- Lennette: No. Politics internally perhaps in the Soviet Union. Sabin went there a number of times.
- Hughes: Wasn't the live vaccine also tried in Britain?
- Lennette: Yes, but the big trials were in Russia.
- Hughes: So with those data Sabin could come back and say that this is what I can do with my vaccine?
- Lennette: Yes, when he had the data showing that the vaccine was effective and was protective.
- Hughes: And then what happened? Was funding immediately cut for the Salk vaccine?
- Lennette: No, I don't think it was ever cut for Salk. Not that I know of. As a matter of fact, when the Salk Institute was put up, this was not Salk's doing. The prime mover of the Salk Institute was Basil O'Connor. We all make mistakes. O'Connor and the top hierarchy at the national foundation came out and said that polio is conquered. This is the year. Let's get the money and have a big campaign. Which is what they did. And afterwards they couldn't garner the money, because everybody took it to heart that polio was conquered. Why should we contribute anything to the March of Dimes? So when the Salk Institute was established in San Diego, they were hard pressed for funds. And then they had to get money from the national foundation, which was more or less obligated to give the institute money for research done by others. After all, they put up this big research institute; somebody has got to pay to cut the grass and pay for electricity and so on. So that's where the money went.

- Hughes: Was the Salk Institute originally set up just to do polio research?
- Lennette: No.
- Hughes: It had a broader mandate?
- Lennette: It had a broader base, yes. Polio was a big part of it, but it was to be more--it was the Salk Institute for Biological Studies. It's pretty unusual to name an institute after a living scientist.
- Hughes: How did the Sabin vaccine eventually make inroads in this country?
- Lennette: Well, everybody decided that the way to go is to use a live attenuated virus vaccine, because then you're going to be producing a good, solid immunity, just as an attack of the disease would.
- Hughes: And did that follow very quickly after the Russian data became available?
- Lennette: Yes.
- Hughes: People could see that the live vaccine really was something good?
- Lennette: Yes. It's not all that clear-cut. We used to think, for example, that smallpox vaccine gave you a permanent immunity just like the disease does. Actually it doesn't. It falls.
- Hughes: Does it fall off?
- Lennette: Yes. The same with yellow fever vaccine. I don't know how many years That's never been quite worked out, although it's a longer-lasting immunity than just giving a dead antigen.
- Hughes: I know the Virus Lab was also involved with a poliomyelitis surveillance program. Was that just an offshoot of the trials that were going on?
- Lennette: Yes. It was an offshoot because we were getting a lot of material from various hospitals, including several down south. We put on these studies in Los Angeles and San Diego using material from patients who ostensibly had a paralytic disease. We found out that this was not polio. This was the first good evidence we had that other agents could mimic poliomyelitis.

Lennette: But the paralyzes that we were seeing were only transitory. They disappeared within thirty days. This became one of the criteria for eventually weeding out true cases of paralytic polio. Did it persist beyond thirty days or not? Not that we discovered this criterion, but other people put it to that use.

Hughes: We've discussed the burden that the polio work put on the lab. Were you able to continue with your other diagnostic work as well as do this?

Lennette: No, it did me in, because up to that point I used to work in the laboratory. The laboratory was small, like the department. And I could work in the laboratory and also do the administrative work. And then when this big polio effort came along, I lost a great deal of time for laboratory work.

And then later when the cancer problem came along, I just became a full time administrator in effect. Cancer virology was another research project that we didn't want. [laughter]

#### Nathalie Schmidt's Polio Research

Hughes: I know it was polio that brought you and Nathalie Schmidt together, a partnership which to some extent continues today. Would you tell me about her, what her background was, and how she came to the lab?

Lennette: Yes. I first met Nathalie in 1953. She came here to San Francisco to one of the microbiology meetings to give a paper. She had gotten her degree at Northwestern University in microbiology in 1952 and then got herself a job at the Evanston General Hospital doing microbiology. At the end of that first year, she came out here to give a paper on the serology of psittacosis and some of the related agents, and did a very good job. Well organized. She presented her material very nicely. As I usually did as a chairman of any scientific session--I still do on occasion when I have younger people coming up to the podium to give a paper--I told her not to get concerned, that if anything developed that she couldn't handle, I would take care of it. Sort of presumptuous in a way, but after you've been through this mill and you get a young colleague who is unsure of himself, or you're unsure of him, you help out. But she didn't need any help. She was poised and did a beautiful job.

Lennette: I was quite impressed with this young lady. At that time I was on the staff of the Highland-Alameda County Hospital, on the infectious disease service with Dr. Joseph Sadusk, who was an internist. I was convinced that there would be a way to develop a diagnostic test for polio. This must have been in the early fifties, '51 or '52.

So I was collecting stools and serial bloods from these patients. I didn't have any use for these specimens since there wasn't any test I could do, except maybe try to get the virus out of the stools. But all this was stashed away in the deep freezer.

We were getting support from the national foundation to develop some of these tests, and I said, Schmidt's the girl. Bright. She's going to go places. So I telephoned her; she had just been looking for a job, and she accepted. I said, "All right, before you come out here, spend about six weeks to two months with Manfred Mayer at Johns Hopkins." (He's the guy who was the complement fixation specialist, basically an immunologist.) "And then come out here by September." She spent about six weeks there, I guess, maybe less, maybe more, at the medical school at Hopkins, and then drove out here. Then I told her what I had mentioned over the telephone, that I thought that we could develop a complement fixation test. "We have all this material stashed away, so here's your laboratory, and here's the stuff, and go at it."

I expected to join her in the lab any day, but I got so tied up with the administrative part of setting up these field trials that I never did, except tangentially.

Hughes: Prior to this there were just the rhesus monkey tests?

Lennette: No. When I was collecting these specimens, tissue culture was already existent. This is the early fifties. We were using tissue culture methods, but with other viruses. We had no support to work on polio. So we were using tissue culture as a basic tool for the isolation of viruses, any virus.

At that time we were kind of naive. We thought any virus would grow in monkey kidney cells or in human cells. We were using human cells also. We had no support for polio until the field trial situation came up. So then we decided we would try to work out a complement fixation test, which we did.\* And then later on this was supplanted by the metabolic inhibition test, which was developed by Salk and the group at Pittsburgh.

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\*Nathalie J. Schmidt and Edwin H. Lennette. "A complement fixation test for poliomyelitis." J. Exp. Med. 102 (1955):133-150

Hughes: Was the complement fixation test widely used?

Lennette: Not too widely, because the metabolic inhibition test came right after that, within a couple of years. The CF test was a fairly good one. That was really the first inexpensive diagnostic test we had. It wasn't all that good, but it was better than what we had. It didn't take a fortune to do the test either. This lab was a routine diagnostic laboratory where things have to be practical. Dr. Schmidt has been with me ever since 1954, when she came to Berkeley as my associate, my co-worker.

Hughes: You said she published a paper on the microfloculation test for poliomyelitis.\* That was in 1959--a few years later. How did one use that test?

Lennette: The antigen was obtained from tissue culture fluid, as was actually the virus.\*\* This was concentrated by high speed centrifugation and used undiluted. Because of the minute amounts of viral material obtainable, capillary tubes were used to perform the test. Dilutions of the serum under test were drawn up into the tube, followed by the viral antigen. Wherever antibody was present, it reacted with the virus and formed a precipitate. This was visible as a line at the interface of the two reactants. Although the technique worked, it was too cumbersome and expensive, but in any case it was short-lived, being shortly succeeded by the micro-neutralization test that I described earlier.

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Hughes: I don't have any more to ask about polio. Can you think of anything to add?

Lennette: Well, I'd like to make one more comment. [reading]"March 14th through 17th, 1983 there will be an international symposium in Washington on the control of poliomyelitis, and to celebrate the conquest of poliomyelitis."

I was in Washington a couple of weeks ago for the retirement party of Dr. Huebner and ran into one of the organizers of this international conference who told me he thought they might have political problems because the auditorium of the Pan American Health Organization building, the Pan American Building in Washington, D.C., may not be large enough to hold all the people

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\*Nathalie J. Schmidt and Edwin H. Lennette. "A microfloculation test for poliomyelitis with observations on the flocculating antibody response in human poliomyelitis." Am. J. Hyg. 70 (1959):51-65.

\*\*Dr. Lennette added this paragraph in the editing process.

Lennette: who want to come. So now they're talking about moving the meeting out to the Clinical Center in Bethesda at the NIH. Apparently the interest and response is very, very good. It'll be a three-day meeting, and it will be interesting to see what happens.

Hughes: That will be a historic occasion.

Cancer Research\*

[Interview 6: January 19, 1983]##

Hughes: How did the Virus Lab become involved in cancer research?

Lennette: The department already had an outstanding tumor registry and a broad overall interest in cancer, almost entirely epidemiological and statistical, but the program was greatly expanded through the insistence and drive of Dr. Lester Breslow, at that time chief of the Bureau of Chronic Diseases. He heard that the National Cancer Institute had money available for research in the cancer field, especially epidemiology. Of course, he's an epidemiologist, and chronic disease is his interest. So he inquired of NCI, and found there were several million dollars that could be made available to the department on the condition that it engage in a very broadly based program. This involved not only epidemiology, but also epizootology--veterinarians would be involved in studying cancer in animals. It would involve chemistry because of the various carcinogens in air, pollutants in water, and so on. And the last proviso was that there be a viral laboratory attached to the program to study the etiology of cancers and tumors, and that it be supportive to the epidemiologic and epizootologic study groups.

I personally was not too interested in getting into the cancer field. I already had my hands full with other things. And, you know, I got into the poliomyelitis studies by the back door. Here again was another instance in which a big program was to be set up, and its establishment depended upon the participation of the Virus Laboratory. There was no way in which this proposed cancer study would be funded without the participation of the Virus Lab. So I had no choice except to go along with it. I had some interest, but it was not a deep interest, in the cancer field.

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\*Dr. Lennette was chief of the Cancer Research Program at the California Department of Health from 1967 to 1973.

Lennette: A large grant application was drawn up, many, many pages explaining what was to be done in epidemiology, what was to be done by the veterinary section, what was to be done by the chemistry section, and by the virus group. This was approved and money was made available, including funds to put up a back building which was to house the cancer project.

#### The New Laboratory Building and Staff Recruitment

Lennette: This is a story in itself, because the funding for that building was to be equally divided between the National Cancer Institute and the State of California. We managed to arrange with legislative people that they would provide half the funds to put up an eight story building which would run from Hearst Street to Berkeley Way. It's a full block wide. It would then house the laboratory which currently existed at that time, plus the new cancer project. This was supposed to have been a matter that was settled and everything ready to go. But when the time came to really implement it, the legislature backed out and failed to keep its promise.

To me this was a very sad reflection on the political process in California, when people can make promises of such a scope and future import and then back out. So what happened, we got a building in the back which is really an aborted building, because it's only four stories high, and it's only half a block long. So when this amputated substitute was further chopped up by the architects in Sacramento who were drawing the plans, (the architects always know more about a building than the scientists who have to work in it), we ended up with one elevator in half a building, which in itself did not really meet the safeguards and the requirements of what was later laid down by the NIH guidelines for genetic engineering, because everybody on these various floors would be exposed to noxious agents, whether they were biological from the Virus Lab or chemical from the chemistry laboratories. But that's the way it was, and that's the way it still is.

As a matter of fact, this was so poorly designed--although the building was put up--I insisted that they make the foundations deep enough that we could put an additional four floors on the top. That has yet to come. By losing the floors, we had no place to house the animals which are so basic to cancer research. We had to go to an expedient of producing what is essentially a sort of mobile home or trailer. We built a dozen of these "pods" and housed them up on the roof of the rear building. Each is a self-contained animal house--air-conditioned, water, electricity, etc.

Lennette: At the end of the wing facing Berkeley Way, the hallway wall was filled in with cement blocks just in case some day the legislature might see fit to expand that building. So provisions have been made for the future.

But we are not in total compliance with the guidelines for recombinant DNA research. In other words, hazards do exist. It was so bad that when the recombinant DNA controversy arose a few years ago, I pointed out to the department, and even insisted, that if anything were done in the development of new laboratories that Sacramento hold not only the responsible scientist, the principal investigator, responsible for anything adverse that might happen in the laboratory, but also there should be a principal administrator, such as the Department of Finance or whoever, who would be equally responsible, because no matter what the scientist wants to do, in the final analysis he has the responsibility but no authority in financial control.

His counterparts on the fiscal and accounting end--Department of Finance and General Services Administration--have the authority but no responsibility. So GSA doesn't give a damn if the building falls apart, if the doors don't work, or the hoods don't function, or the stacks don't have air destructors. It's of no great moment to them. And that's where the problem lies. It isn't with the principal investigator; it's with these people who are not knowledgeable and who tend to put their money elsewhere.

Hughes: How can an unsafe building, particularly as part of the California State Department of Public Health, continue to violate the guidelines?

Lennette: The sovereign State of California inflicts rules, laws, and regulations on everybody but itself. [laughter] They're always exempt from everything, just like Congress. As an example, now this week they want to make everybody covered by social security, with the exception of Congress. They always leave themselves out. So that's how it goes.

Hughes: And what exactly did the Virus Lab do as far as cancer research is concerned?

Lennette: We didn't have the staff to do this, because the staff was so small at that time, concerned with other matters. We couldn't give up the things we were doing. We were heavily involved in viral diagnostic work. I'm talking now about '64, '65.

Lennette: So I recruited additional staff. Natalie Cremer came on the staff as the immunologist. She had been highly recommended to me by Dr. Dan Campbell of CalTech, with whom she had spent several years as a postdoctoral student. Very bright. Very highly regarded. I approached Dr. Campbell at an immunology meeting--I think it was down in Santa Barbara or somewhere in that area--told him I was looking for an immunologist. He said, "I've got the very person you need." And I said, "I think you're talking about Natalie Cremer." He said, "Yes." I said, "I'll take Natalie. I'll offer her an appointment." I had never met her. On the strength of her recommendations, not only from him but also from the man under whom she had received her doctoral degree, Dennis Watson at the University of Minnesota, I felt she was the logical person. And she's a very fine immunologist.

Hughes: Didn't John Riggs come at that time?

Lennette: John Riggs came about the same time. The kind of work we were doing required somebody with a good background in virology, but he had just done a great deal of work on fluorescent antibody techniques. As a matter of fact, he's the one who devised the fluorescein conjugate that's widely used today. So I offered John Riggs a position on the staff, and he came to us from Ann Arbor--the University of Michigan--to work on the viral etiology of cancer.

Hughes: So those two were...

Lennette: Those two were the laboratory people whose main concern was with cancer.

Hughes: Do you remember what aspect of the cancer problem they were working on?

Lennette: Natalie got involved in leukemias, and John, with whom I had somewhat closer contact...You must remember, I was primarily an administrator; I was not a worker at the bench, just sort of an overall supervisor, and I had a lot of responsibilities. I worked more closely with John because he was doing fluorescent antibody work, and we were looking for an antigen which other people described...

Let me back off a little bit. In Houston a zoologist thought that viruses might be involved in the causation of cancer, so he ordered from the American Type Culture Collection a vial, an ampoule, of adenovirus type 12, which he received, which he opened, aspirated into a syringe, and inoculated a number of hamsters, and these animals came down with tumors. So he showed that adenovirus was oncogenic. Now this is not good microbiology. It might be good zoology. [laughter] This is not the way you do microbiology, for a number of reasons. Anyway, he did get tumors, and this opened up a whole new field.

Robert Huebner, the National Cancer Institute, and the Viral Cause of Cancer

Lennette: Bob Huebner, who is one of the leading spirits in contending that viruses must play an important role in the causation of human cancers, with which I concur, also began to study the adenoviruses as a group.

Hughes: Now are you saying all human tumors are caused by viruses?

Lennette: No, no. That there must be some human... Why would nature be so selective that viruses produce tumors only in avian species or in animals and not in man? Man is no different. So at least some cancers must be produced by viruses. Or maybe they all are, not directly by the intervention of the virus, but maybe the virus triggers some mechanism whereby genes are de-repressed and become active, because man now, we know, carries so-called oncogenes, which are components of a normal cell, and, if they're allowed to express themselves, result in the production of a cancer.

Huebner was quite sure that some of the cancers are caused by viruses. Here was an illustration of a virus producing a tumor in a rodent. Let's see if we can get any evidence whether adenoviruses are involved in the causation of human cancers.

So it was shown by his associates and others that early in the infection the virus produces an antigen called T-antigen. You can find this antigen in animals. We spent a lot of time looking for T-antigens in humans, but of course never got any evidence that this was any sort of a real phenomenon. It was this sort of thing we were doing in the cancer area.

Then there were also other aspects in the cancer field, looking for leukemia viruses. For example, veterinarians were studying the occurrence of leukemia amongst cats, and what relationship this might have to the occurrence of leukemia in families. So we were inoculating cats with material from ill cats to see if we could reproduce the disease, and what the course was, this sort of thing.

Hughes: I didn't notice very many papers published on the subject of cancer.

Lennette: Everything was so negative. This is why I didn't want much to do with it, because it was such a difficult field to work in. And it still is. I guess it will be until the molecular biologists give us some more tools, more mechanisms to deal with.

Hughes: How did the NCI [the National Cancer Institute] regard the research on the viral cause of cancer?

Lennette: They regarded it as a very important area which should be investigated, and I think that philosophy arose through the personal efforts of Dr. Huebner. He was very voluble, very vociferous, very persuasive. He knew a lot of people. He travelled all over the country. He talked to people. And he felt that something ought to be done. So what he did was convince the NCI bureaucracy, the administrative people, people who made the decisions, that money should be allocated for cancer research.

Originally he was with the National Institute of Allergy and Infectious Disease, and complained very bitterly that he didn't get sufficient funds within the institute for the work he wanted to do. Although in actual fact, when he looked back at it some years later down the road, he realized that they had given him a very big piece of their budget each year so that he really had no basis for complaint. He admits that. He's a very honest person.

But because he felt that he wasn't getting enough support monetarily from NIAID, he went to NCI, where he could get more money because cancer was the big field at the time. Anything that the cancer institute asked for from Congress, it got, plus more. As a matter of fact, for a while they got so much money, they didn't know how to spend it. The virus cancer program came at the right time, was easily funded.

Huebner served a very useful and essentially a unique role, because he travelled, not only here but also in Europe, occasionally in Japan, and had a lot of laboratories collaborating with each other. He had a whole network. He sat on top of all this, and it's remarkable how he could keep this juggling act going. He talked to people to see what they were doing, remembered what they were doing. And I'm talking about dozens of laboratories. He knew what everyone was doing, and the relationship of that facet to some other facet. So he did a real service in coordinating much cancer virus research.

It was he and his associates, George [J.] Todaro primarily, who came up with the oncogene theory of cancer. This wasn't too widely accepted or too highly regarded at the time, but today it's generally accepted that oncogenes, which occur in man, are part of the evolutionary history of mankind and animals. They do occur in man, and they play a role. Now what the role is, whether it's a de-repression that sets off promoters or initiators or whatever has yet to be determined. There's no question that oncogenes are present because you find the same genes in cancerous animals.

- Hughes: That's interesting.
- Lennette: So our published contributions are relatively minor and scarce, because the field is just difficult. It's a hard row to hoe.
- Hughes: You made a survey in 1965 which was called a survey of the tumor virus problem. It was published in Cancer Research.\* It was obviously part of a symposium.
- Lennette: I think that had to do with the adenoviruses, as I recall. I'm not sure.
- Hughes: You refer to a Dr. Rowe. I believe he had made an address just before you.
- Lennette: Wally [P.] Rowe. He had done a lot of work on adenoviruses, both as respiratory disease agents and etiologic agents in experimental cancers in animals.
- Hughes: It sounded as though he had just presented a paper on viruses as a cause of cancer in humans. Is that possible?
- Lennette: Probably, because he was very much involved in viral cancer research, especially from the genetic side.
- Hughes: You concluded that more research was needed on the relationship between viruses and cancer.
- Lennette: We were never able to show any definite relationship between the occurrence of T-antigen in man and cancer.
- Hughes: Do you think the fact that you were getting mainly negative results influenced NCI as far as support for future research was concerned?
- Lennette: No, I think NCI was finally dissuaded from supporting work in the virology area to such a great extent. I think the chemists, who had always had the field to themselves, the biochemists and organic chemists primarily, felt that the money was being misspent. I'm not saying this critically. I think they honestly felt that way, that there was no really good evidence that we should be spending money on viruses and cancer. But my position was, we don't know. Let's find out. If it's negative, we'll just stop. But it eventually got to the point where it was not productive, and I think that the people who were supportive of the chemistry area won out.

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\*Edwin H. Lennette. "Formal discussion of: A survey of the tumor virus problem from an epidemiological standpoint." Cancer Res. 25 (1965):1286-1288.

Lennette: This is not unique. If you talk to people in the Environmental Protection Agency, you'll find that the consultants and the staff are mostly chemists--analytical chemists, organic chemists, physical chemists, a few biochemists--and engineers. A biologist is a rare animal. And an M.D. is practically nonexistent in the EPA. And yet here they are confronted with many medical problems, and they need medical consultation. Also they forget that many of the pollutants are not physical or chemical; they're biological. So some day they're going to have to wake up to that.

#### Fads and Fancies in Cancer Research

Hughes: Is the name Michael Shimkin familiar to you?

Lennette: Mike was one the the high-level administrators, a very capable person, within the NCI. Eventually he retired and went to the University of California at San Diego and did very well there. A very personable, very knowledgeable scientist.

Hughes: He's written a fair amount on the history of cancer research, and has a theory that, beginning more or less at the beginning of this century, there are phases that cancer research goes through.\* In the beginning, there was a rush with the transplantable tumors. And then tar-induced tumors. And chemical carcinogens. And then by the 1940s there was more emphasis on chemotherapy. By the late 1950s, he says, there was a renewed interest in the virological and immunological aspect of cancer research. I guess harking back to Peyton Rous.

Lennette: Peyton Rous' work back in 1908 or 1909.

Hughes: Yes, with the chicken sarcoma virus?

Lennette: Yes, Rous sarcoma virus. Well, that work was very widely discredited, not in the sense that it wasn't well done, but, what does it mean? It has no bearing on human cancer. Well, here's an individual who really opened up a field, far ahead of his time. He should have received a Nobel Prize right away. But for many, many years he was just bypassed.\*\*

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\*See for example, M.B. Shimkin, "Neoplasia." In: Advances in American Medicine:Essays at the Bicentennial, N.Y.: Josiah Macy Jr. Foundation, 1976, vol.1, pp. 210-250.

\*\*Rous received a Nobel Prize in 1966, fifty years after the discovery of the chicken sarcoma virus.

Lennette: So it shows you the chances of getting a Nobel Prize. A lot of it is luck. And a lot of it is the times and politics. What you were just saying, sure, the cancer field, like everything else in medicine, and in other areas of science, has its ups and downs. There are fads and fashions. And, I think, in the early 1950s we didn't know too much about virology, but every other lead, chemical and otherwise, had been pretty well exhausted. People were just sort of grinding the crank. So let's take a crack at virology.

Well in the 1950s we didn't have too much in the way of methods. It wasn't until we got into the sixties when the molecular biologists, biochemists, and geneticists working together opened up the field and gave us the tools. And then virology went ahead by leaps and bounds, and these new developments gave impetus to the search for viruses, because you had markers, tags, a way to determine whether a virus was present or not, Mike was quite right, that these things do change. We have fads and fancies in medicine.

Hughes: One last question on cancer. As you well know, in 1971 Congress passed the National Cancer Act. Did that have any repercussions on the institution here or what you were doing? Did you ever dabble in cancer research again?

Lennette: No. The only thing I had to do with that cancer act was appear at the White House when Mr. Nixon signed the bill, and I got one of the pens as a souvenir, which I still have at home.

Hughes: Was that because of your former work?

Lennette: Because we had been working in the cancer field. There was quite a motley group at the White House at the signing of the bill. President Nixon had some of the senators and congressmen behind him when he sat down to sign the bill. Then his staff passed out souvenir pens for those of us who were present at the time. That bill, of course, made money available for cancer research.

Congress always has its pets, too, and sometimes it's very unfortunate, because you get somebody who's highly visible and is very persuasive, and the first thing you know, you have a new institute founded, but with no money to support it. So the money has to come from the others already existing, or they will take an institute and tag on another disease. The age group of Congress is such that they're all dying off of something or orther, and each congressman has his own pet disease that he wants worked on because he's afraid of dying of something or other.

Evolution of the National Institutes of Health\*

Lennette: The National Institutes of Health are an invaluable asset to the nation. The forerunner to the institutes was the old Laboratory of Hygiene, which was established in a small room at the Marine Hospital on Staten Island, New York by a young Public Service officer named Joseph Kinyoun. He studied in Europe under a number of greats such as [Robert] Koch, [Paul] Ehrlich, [Emile] Roux, [Emil] von Behring, and his small laboratory probably was the very first bacteriological lab in this country.

As the headquarters of the Public Health Service shifted about in Washington D.C., the lab had several homes. The present site of the National Institutes of Health in Bethesda arose through gifts of land by the Luke Wilson family, father and son. The original gift of forty-five acres was later supplemented by additional donations of land, eventually attaining ninety acres. The National Institutes of Health occupied crowded quarters at 25th and E streets NW, and it was decided to use the Bethesda site as a new home. Buildings were erected on the Wilson-donated land, and NIH moved to its new and present home in 1938. Over the years, much additional land was purchased to accommodate growth of the institutes, the present site occupying some three hundred acres.

Incidentally, yesterday in Bethesda, Building One, which was the first building, the administrative building, was named after Dr. James Shannon. He was the director who really built up, in his sixteen years or seventeen years of service, the National Institutes of Health. He should get the credit for building the world's finest research institute for medicine and public health.

Over the years, there was a series of directors, and the institutes grew building by building. So when Jim Shannon took over--it must have been the sixties--he eventually formed a very close relationship with Senator Lister Hill of Alabama and Congressman James Fogarty from Connecticut. The three of them made a very good triumvirate, because Jim had a lot of ideas. He had a lot of vision. He got great support from Lister Hill and great support from Fogarty. They are the ones who got money to put up the buildings, to enlarge the staff to its present size, which is around ten thousand people, plus all the research buildings, and the huge clinical center.

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\*Dr. Lennette added the following two paragraphs in the course of editing.

Lennette: The various institutes with time developed a worldwide reputation for outstanding research, and because they were so well financed by Congress, they attracted many young scientists in the biomedical field who came as postdoctoral investigators and either were appointed to the staff after their apprenticeship or went into academia.\* This graduate training program was a fortunate development, because President Franklin Roosevelt and his New Deal over the years raised taxes so high that philanthropy became almost nonexistent; universities which depended on the largesse of philanthropists such as the Rockefellers, the Swift family, the Rosenwalds and others, now had to look to the National Institutes of Health for funds to support basic biological and biomedical research. This led to the establishment by NIH of pre- and postdoctoral training programs in the universities and medical schools, and to fellowship programs and research grants.

Hughes: So that came later? NIH was a research organization before it was a funding source?

Lennette: Essentially, yes. Congress, through the leadership of Senator Lister Hill and Congressman James Fogarty, provided the money that Jim Shannon needed to set these programs in motion. They were established virtually simultaneously. Congress legislated the formation of a national advisory council for each institute, and the institutes as a whole set a series of so-called study sections that spanned the field of biomedicine, for example, the Virology and Bacteriology Study Section, established in 1949, which later, with the burgeoning of the biomedical research establishment in this country, split into virology and bacteriology.

The Virology and Bacteriology Study Section was one of the very first set up, and Dr. John Paul, professor and chairman of the department of preventive medicine at Yale Medical School, was the first chairman of the study section. I was appointed co-chairman the next year; we shared the task of running the section until John withdrew the following year, and I served as chairman through 1956.

I later, in the early 1960s, was appointed to a four-year term on the National Advisory Allergy and Infectious Diseases Council, which gave me an opportunity to express my dissatisfactions and reservations and misgivings about some of the NIH programs. I have mentioned the postdoctoral research and teaching programs.

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\*Dr. Lennette inserted the following remarks on NIH after the interviews had been concluded.

Lennette: I questioned the need for so many scientists in biomedicine and how they would all find positions. I was repeatedly told by my colleagues that I did not understand academia and academic medicine, that these young people were needed to staff research projects and to teach. Well, the day of reckoning came in the late 1970s when NIH budgets suffered severe cutbacks, and many faculty members and researchers all over the country supported by "soft money" lost their appointments. The School of Public Health at the University of California at Berkeley, for instance, reputedly lost some twenty to twenty-five percent of its faculty!

I won't get into all the criticisms I have of how teaching is being done today, but I think it's pretty slovenly, in the graduate school.

As to research programs, Dr. Clayton Loosli, dean, School of Medicine, University of Southern California; Dr. Leon Schmidt, director of the National Primate Research Center, University of California at Davis; and I, all serving on the National Advisory Allergy and Infectious Disease Council, tried to persuade the National Institute of Allergy and Infectious Disease, at that time under the directorship of Dorland J. Davis, to set up an in-house program on chronic disease, but to no avail. Some years later such a program was established within the National Institute for Neurological Diseases, and several people moved from the Allergy and Infectious Disease Institute to Neurological Diseases--among them was Carlton Gajdusek, who eventually was awarded a Nobel Prize for his work on chronic viral infections, so-called "slow virus" infections, of the central nervous system.

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#### Rubella Research

Hughes: You and Dr. Schmidt began to publish on rubella in 1966. Could you tell me how you got into that line of research?

Lennette: Well, it's a philosophical matter really, because, as I said, we set out to operate a viral diagnostic laboratory, which meant that as new developments came along, we had to be aware of them. We had to know what they were, how they functioned, and the best way to find out is to do it yourself.

## The Premarital Test for Rubella

Lennette: So when rubella virus cultivation was described by two different groups back East, by Tom Weller and Frank Neva at Harvard, and Paul Parkman et al. at Walter Reed Army Institute of Research, we got the information from them of what cell line to use, how to grow the virus and how it behaved in culture. Then Nathalie Schmidt began to work with the virus to get familiar with its peculiarities, idiosyncrasies, and foibles so we could coax the virus to grow in these and other cells. The idea was that when she knew how to do this, she would then take one or two technologists in the laboratory, train them in the methods, and then we would initiate rubella diagnostic tests. It turned out that other people, of course, were interested, too, in rubella, which is an important illness. It's universal; at least eighty percent of people have antibody by the time they are adolescents.

There are a number of different serologic techniques developed for diagnosis, and naturally there were problems. To iron this out, and get some sort of standardization, a number of laboratories were invited by the Center for Disease Control to run a series of tests the way they were doing them in their own laboratories. Then we would make comparisons to see what kind of answers we would get. The results were pretty bad! Everybody varied all over the place. Obviously something had to be done to standardize, and that in itself took several years, but eventually it was pretty well worked out. Then CDC, being a national laboratory, a national resource, drew up the standard protocols for doing the tests, and from that came the viral diagnostic test for rubella, which was a hemagglutination inhibition test.

This made it possible to test women for the presence of antibody to determine whether they were relatively safe from infection, because if infection is acquired in the first trimester of pregnancy, it may lead to genetic defects in the newborn. Hence, to avoid all of this fetal wastage, it was decided that every woman of childbearing age ought to have a premarital test done. In California this was carried over into a law that made it mandatory that every woman in this age group had to have a premarital test done for rubella. I was never entirely convinced that this was the way to go, but the infectious disease people (the pediatricians) won out. That's another story. But anyway, the law was passed, and we had to do the tests.

Now that has an interesting spinoff, too. Mind you, this laboratory was the first real, specialized civilian viral diagnostic laboratory in the country. Other smaller ones had subsequently sprung up, but nobody was in a position to do very much work, because viral reagents or antigens, specific immune sera, were not available commercially. We tried repeatedly, Schmidt and I, to get manufacturers to make these reagents.

Lennette: The answer being, "There's no point in that. There's no money in viral diagnostics. There's no market. Nobody's going to buy this stuff." It's a catch-22. If you make it, people will buy it. But there's no demand because the material is not available. So they were never very interested.

#### Diagnostic Kits

Lennette: Now here comes rubella. All of a sudden all of the pharmaceutical houses are interested, because every woman in the country is going to be tested for rubella. "My God, look at the size of that market out there. We ought to go in and cut off a big piece of this pie for ourselves. This ain't nickels and dimes; it's millions."

So what happens, they sit down to make diagnostic kits. "You don't have to know any virology. Just buy our kit, read the instructions, which we make very simple so that you can understand them, and do the tests; that's all that's required."

Hughes: So any G.P. [general practitioner] could do it?

Lennette: Any technician--ostensibly, you could bring a kid in off the street and she could run the test for you. She didn't have to know any virology. Which of course is incorrect. You have to have some kind of a basis upon which to make judgments and interpret results. According to these people, you didn't need that.

So a number of them got into the act. They began to make kits. Well, we and other laboratories got involved in testing some of these to see how good they actually were, and they were pretty good after a while. They made a lot of missteps early on, but they improved as they went along and got experience.

Then comes another highly important disease, hepatitis. Hepatitis can now be diagnosed by picking up the surface antigen of the virus in the blood; hepatitis B virus I speak of. With this step forward, you now have a viral marker that you can really pick up. All these biological houses now jump into making kits for the diagnosis of hepatitis B.

Then along comes herpes genitalis. Start making kits for that. What I'm saying is that nobody really cared one iota about making diagnostic reagents for the laboratory until the high-volume diseases came.

Lennette: The incidence of hepatitis, of rubella, and now of cytomegalovirus, for example, and of herpes genitalis, is so high that these people are now making kits for diagnosis of these infections, because there's lots of money involved. I understand the market for hepatitis B kits alone is close to one hundred million dollars.

But there's a whole plethora of other viral diseases for which nothing is being made, because there's no market. This is similar to an article that Judy Randall wrote a while back. I think it was in California Magazine. Judy, who is a science writer, called these "orphan diseases." These are diseases of so little occurrence or are so obscure that no biological house bothers to make either a vaccine or look for a chemotherapeutic agent. So they ignore these diseases, and the same thing happens in diagnostic virology. There's a big market there if you want to go after it.

#### The Premarital Test for Rubella (continued)

Hughes: Could we go back to your skepticism about the premarital test for rubella? Would you tell me why you didn't think the law was a good one?

Lennette: I don't like to see laws that make it mandatory for people to do things. I think that ought to be a matter of choice. I think people should be informed--and they have been--of what the consequences of a rubella infection are. The question arose, if women do acquire rubella, what's the proportion of people who will be adversely affected with respect to the fetus? We really didn't know, but were sure it would be high.

So I thought to make this mandatory for women was premature, and it would be better to give the vaccine to school children along with other immunizations. So did the department, as a matter of fact. What happened, there were one or two people in the department who were really gung ho to get this law, and they managed through nondepartmental channels to convince key legislators that this is what we needed, and that's what we got. In this country with all of our crazy ideas about civil rights, welfare rights, and so on, I guess the males could yell that they're being discriminated against because they aren't vaccinated.  
[laughter]

Hughes: Was the lab ever involved with the production of a rubella vaccine?

Lennette: No. That was done mostly by the people at the Bureau of Biologics. There were others who worked on vaccines, too, but Harry Meyers and Paul Parkinan of the Bureau of Biologics produced a very good vaccine that was used,

#### New Techniques and Rapid Diagnosis

Hughes: You published on immunofluorescent techniques to be used for the identification of the rubella virus.\* Were those techniques actually developed here at the lab?

Lennette: Yes, in large part. Prior to that we had to use interference tests, so-called, to see whether the virus was growing or not. And that took time. The virus was relatively slow growing and you had to do the interference tests using another virus to see whether there would be interference with the growth of that second virus. These were indirect methods. Then if you could develop a method where you put, let us say, a throat washing, a throat swab, into tissue culture, let it incubate for a few days, and then stain the cells with antirubella serum to see whether you've got any antigen present, that would be the way to go.

Incidentally, we did that with respiratory syncytial virus, which is probably the most important virus of infancy. This virus produces a very high mortality in infants under one year of age. What we did was get throat swabs from the infant, put them into some sterile culture medium, and then put the culture medium into tissue cultures, and then within a matter of six or eight hours stain those cells with fluorescent antibody and see the virus antigens. That's rapid diagnosis.

This is what we've always tried to achieve, rapidity. An answer two weeks from now doesn't help very much. However, this being primarily a public health laboratory, we were oriented to supporting the epidemiology people. Well, when you're doing an epidemiological study, you don't care, relatively, when you get the answer. Time is not important. But to a clinician who is treating a

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\*Nathalie J. Schmidt, Edwin H. Lennette, James D. Woodie, and Helen H. Ho. "Identification of rubella virus isolates by immunofluorescent staining, and a comparison of the sensitivity of three cell culture systems for recovery of virus." J. Lab. Clin. Med. 50 (1966):502-509.

Edwin H. Lennette, James D. Woodie, and Nathalie J. Schmidt. "A modified indirect immunofluorescent staining technique for the demonstration of rubella antibodies in human sera." J. Lab. Clin. Med. 69 (1967):689-695.

Lennette: patient, he's got to have an answer stat. So this is now the big push, to get a test which is quick. That's the emphasis today, rapid diagnosis.

To hear some of the people talk about rapid diagnosis in meetings today, you would think they'd invented the field, or that it is something that is new that has just been discovered. Well, people in the viral diagnostic field have been thinking of this for years! They just haven't had the way to get at it, nor, for that matter, monetary support.

Hughes: What are some of the new techniques that make diagnosis faster?

Lennette: There's an enzyme technique called the ELISA test. Well, there was a radioimmunoassay, for example. That's expensive because you have to use radioactive material. Here you buy an ampoule of radioactive reagent, and unless you're doing a big volume of tests, this test isn't feasible in a small hospital, because you end up having to discard the unused kit reagents at the end of a month or two months, whatever it is, and so the cost is very high. There is also the matter of personnel hazard and disposal of the radioactive waste material.

Radioimmunoassay in virology has just sort of disappeared. It's been replaced pretty much by immunofluorescence techniques and by what we call immunoenzymatic methods. You hook an enzyme onto a known antibody as a label, then mix with the clinical specimen containing the suspect virus. This mixture is then incubated. You add an indicator substrate, and if the enzyme is free, it works on the substrate and then there's a color change. A very simple test, and one that's very effective.

Hughes: Did this lab have any part in developing that?

Lennette: We didn't do much in development. We've made some changes. We keep modifying it, because many of these things, until recently, were done in small research laboratories. Somebody would write a paper, "Here's a new technique and we just tried this out on eight or ten patients," or whatever it is, and they produce a very profound paper.

That's not the proof of the pudding. Anything statistical has got to have a big background. This laboratory sits down and does a hundred or two hundred patients, and then evaluates it statistically and says, "This is a good test," or "This is a bad test." Or if we see difficulties, we try to iron out what the problems are, always keeping in mind that if we can iron out the difficulties, we can adapt the test to use in a smaller laboratory in the county, not necessarily a hospital, but a small lab. After all, everybody doesn't have a staff of a hundred people. Even in

Lennette: a hospital, they may have a staff of five, and one of them is the virologist. Usually, she doesn't have much time, so you have to make the test simple, avoid labor-intensive methods.

Hepatitis Research (continued)

Hughes: Well, on to hepatitis. Primarily you and Dr. Schmidt were the names on the papers.

Lennette: Early on we worked together on hepatitis tests, and then Schmidt did most of the research herself.

Hughes: And that began about 1970?

Lennette: Just about the time that hepatitis B virus was found to have a surface antigen. The whole field was really opened up--again it's a matter of serendipity--via Baruch Blumberg. Baruch is a geneticist, not a virologist or a microbiologist. He was studying the blood bank bloods and noticed a strange antigen, when he was typing out these bloods, in the serum of an Australian aborigine. This seemed to be a unique antigen, so he called it Australia antigen.

Later on it was found that this antigen occurs in the blood of patients with hepatitis B, and it was a real distinctive marker. The scientific community saw, by electron microscopy, the presence of distinctive particles in these bloods, which are now referred to as the Dane particles, and which represent the virus. The S antigen represents a lot of leftover pieces, as in an assembly plant, you make too much of something and it's left over.

The S antigen was the marker that could be used for diagnosis because it's easy to pick it up serologically. So a serological test was developed to pick up this HBVs antigen, hepatitis B virus, S antigen. Of course there are other antigens, too, such as a core antigen, the E antigen. These too, then, made feasible the diagnosis of hepatitis B and permitted people--for example, our own infectious disease section--to do epidemiological studies with some assurance.

Well, then a lot of refinements were made. At first we started out with some intricate techniques. Then we finally got down to the simple ones. And from that came worldwide the observation that HB virus formed only part of the whole hepatitis picture. There's another very important virus, hepatitis virus A, HVA, which is what everyone is working on, that accounts for

Lennette: a certain proportion of cases. But the preponderance of cases of hepatitis are caused by what is called non-A and non-B. Maybe eighty percent is caused by this unknown agent, transmitted primarily by transfusion.

Hughes: Is that a virus or viruses?

Lennette: The NIH group thinks so, because they inoculated some of this non-A, non-B blood into chimpanzees and produced disease. They don't know whether it is one virus or whether there are subsets. That's a whole new area. More recently, a new hepatitis agent, the delta virus, has been described from Italy. It is a so-called incomplete virus and requires HBV for its replication.

Hughes: Sounds like the early flu studies.

Lennette: Well, that sounds like Horsfall and Lennette about 1939, 1940, when we devised the nomenclature for influenza. The first one was influenza A. Then Tommy Francis found another virus, which we then called B. Then all the rest were non-A and non-B.

Hughes: That's what I was thinking of.

Lennette: That's the logical way when you don't know much about the field.

Hughes: Anything more about hepatitis?

Lennette: No, except that it's a very important disease. Well, hepatitis worldwide, I guess, is just second to malaria. Malaria is probably the most important. I think it is without exception the most important disease in the world. Millions of cases. And hepatitis is pretty close behind in incidence.

Hughes: You're talking now about infectious diseases?

Lennette: Yes.

#### Laboratory Personnel and Miscellaneous Research

Hughes: The catch-all of "miscellaneous research," if you don't mind the term. I'm not demeaning the research by calling it that.

In the 1960s, there was a large influx of people into the Virus Laboratory. We've talked about some of those people. It seems to me the research branched out into several directions. Some of the people who came around and about this time were Robert

Hughes: Magoffin, Rex Spendlove--we talked about him when we were talking about the reoviruses--Jack Schieble, and James Chin. I thought we could talk about their positions in the lab and what research they were doing.

Robert Magoffin and Laboratory Administration

Hughes: Robert Magoffin interests me because apparently he was assistant chief of the Virus Lab?

Lennette: [nods]

Hughes: He was hired to fill that position?

Lennette: No. He came to the department after the war. He was a naval officer. He received his medical degree at the University of Texas at Galveston, then went to Minnesota and worked on brucellosis with Wesley Spink who was one of the nation's authorities on brucella. So during his residency under Spink he learned a fair amount about infectious disease. Then he came to this department, and worked in the infectious disease section. This is in the early fifties. When the polio business came along, he was involved as a sort of team epidemiologist to help in our studies, and then eventually I took him over as part of the Virus Laboratory staff.

He was a very, very bright young man, who had good sense, was dependable, and was very analytical, wouldn't accept anything unless he felt that it had been looked at thoroughly and was scientifically acceptable. He was a very valuable asset, a good right-hand man. Anyway, over the succeeding years, we developed a good working relationship, a good working partnership.

Hughes: Are you speaking from a research standpoint or from an administrative

Lennette: Administrative. No, I did no research personally at the bench with Magoffin. Administratively, I was responsible for running the laboratory and for doing all the planning. And for doing all the dislikable things that an administrator has to do, whereas Bob never liked to get involved in anything unpleasant. We made plans; he would see that they were executed and followed through. He was a good number two man. We made a good team. I did a lot of travelling in those days, eighty, ninety, hundred thousand miles a year. When I was away, he ran the laboratory administratively and did a very good job because he knew how I would react to things. And Nathalie ran the laboratory side.

During the polio years we accumulated a lot of information on the occurrence of polio, a lot of epidemiological background. That was the substance of the manuscripts that we published on polio. He at that time was still part of the infectious disease

Lennette: section, but when he moved over to the Virus Laboratory, we still used those data. We pooled them. We published, for example, one paper which is fairly important,\* and that was to show that mumps virus can produce a disease indistinguishable from paralytic polio, except the paralysis is transient, and after about thirty days it disappears and the individual recovers. Nobody had ever looked at this sort of thing before.

So we had a number of these, what you call miscellaneous, things that were just observation that you picked up, a sort of serendipity. And there were others of a similar nature. Some were about the coxsackie viruses. Hand and mouth disease was a coxsackie virus infection that we described. This, too, was just purely coincidental. The laboratory was getting all this material from these individuals with hand and mouth disease, and we isolated coxsackie viruses. Ours was one of the first descriptions of the disease. We and a Canadian group about the same time described these episodes. It's commonly accepted now that the disease has a viral etiology.

And we did some work on epidemic pleurodynia, which is another coxsackie virus infection. We had several episodes here, and we had a young public health resident who worked with me by the name of Robert Gordon. We did a couple of minor studies, not very good ones, because we didn't have the base, on myocarditis due to coxsackie viruses.\*\* That etiologic relationship is of course well known today.

More on Rex Spindlove and the Reoviruses

Lennette: Now with respect to Rex Spindlove, he worked on the reoviruses, which were not very well known at the time. And I think his greatest contribution was to show that the virion has two layers, two shells around it, and that you can increase the infectivity if you break down, by enzymatic processes, these protective shells. It's like a nut inside of a walnut shell. If you break these down, then you release the infectious moiety, and the titers go way up.

Hughes: And he did that chemically?

Lennette: Yes, enzymes. Papain, trypsin, chymotrypsin.

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\*Edwin H. Lennette, Gerald E. Caplan, and Robert L. Magoffin. "Mumps virus infection simulating paralytic poliomyelitis. A report of 11 cases." Pediatrics 25 (1960):788-97.

\*\*Nathalie J. Schmidt, Robert L. Magoffin, and Edwin H Lennette. "Association of group B coxsackieviruses with cases of pericarditis, myocarditis, or pleurodynia by demonstration of immunoglobulin M antibody." Infect. and Immun. 8 (1973):341-48.

## Lyndon Oshiro and Electron Microscopy

Lennette: One other valuable thing is that Rex had working with him a young postdoc by the name of Lyndon Oshiro. Rex was doing a certain amount of electron microscopy using the microscope up in the Virus Lab on the University of California, Berkeley campus, catch as catch can. He had a chap here, a visiting scientist, by the name of Singer, who was a very eminent scientist, physical chemist as I recall, who was working at the Scripps Institute in La Jolla and who was at CalTech for a while. Singer had to use the 'scope up on the campus, and as a result Lyndon was able to get in and photograph his material and learn something about electron microscopy; he got very much interested and took to it.

I later arranged for Lyndon to go to Columbia University and work with Councilman Morgan, who was one of the outstanding electron microscopists in the country. Lyndon spent a year there in electron microscopy, and since then has become one of the pillars of the cult of electron microscopists. He does beautiful work, magnificent work. Very careful, very meticulous, and now he's well recognized. He has an excellent reputation, and is always being offered appointments elsewhere.

Hughes: Is this the point to say something about the contributions of electron microscopy to virology? Before the arrival of electron microscopes with the ability to give the resolution that one would need to see a virus in detail, there was only speculation about the anatomy of a virus.

Lennette: When I went into virology, and for some years afterwards, a virologist was pretty much in the same position as a physicist. The physicists could postulate the existence of certain size particles, molecules, atoms, ions, or whatever they call them today. And we were in the same boat; except for the larger viruses like vaccinia or molluscum contagiosum, we couldn't see any viruses under the light 'scope. And then along came the electron microscope, back in the early thirties, out of Germany. It was pretty crude. As I said once before, you could magnify a banana a thousand times, but the resolution just wasn't there. You just got a great big banana that you could look at, but you couldn't see the pits or the holes or the seeds or anything else.

But over the years, with the interest of physicists and biophysicists, the instruments were further and further developed, and included contributions from the people here at Berkeley on the campus, Wendell Stanley's group--mainly Robley Williams.

Lennette: Williams was the microscopist, and an interesting person. He came from the University of Michigan where he had been trained as an astrophysicist. From astrophysics he got into electron microscopy and became a recognized, internationally renowned authority. Lyndon had some exposure to him up there before he went to Columbia.

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Electron microscopy's usefulness is illustrated by the fact that if it weren't so expensive it could be widely used to examine clinical materials, for example, the presence of rotaviruses in stool material. Do a quick emulsion and look at it on the grid under the 'scope, see the particles present, and in a matter of a few hours you have a diagnosis. That's too expensive a piece of equipment for routine use. So we use other techniques. But it is invaluable in many of our research projects, so we know what we're doing. And, I guess, as we get more and more potent instruments, we'll be able to see down inside the viral particle itself.

Jack Schieble, James Chin, and the Fort Ord Studies (continued)

Hughes: Jack Schieble.

Lennette: Schieble was at the University of Michigan in the laboratory of the department of epidemiology, School of Public Health. He was one of Thomas Francis' students and received his Ph.D. under him. He and John Riggs were there at the same time. I had talked to both of them about coming here. I was interested at that time in getting somebody to run a laboratory for our respiratory disease studies, who could spend a lot of time down at Fort Ord. This ties in with Jim Chin, whom we mentioned. Jim had been trained in infectious diseases, and also in epidemiology, and he was picked up early by the Hooper Foundation people, who recognized his potential. Jim worked in Kuala Lumpur, where the university had a field project going. Jim was there for several years, and got some very good background, and very good training.

##[tape interruption]

When that project folded, Jim was at loose ends. I knew of him by reputation, because I had heard a great deal about him from K. F. Meyer and the other people at the Hooper Foundation. So when Jim came back to the Bay Area, he was just the person we needed--a good epidemiologist, good clinician. He would be the person to run the operation at Fort Ord, and Jack would be the guy to run the laboratory here in Berkeley.

Lennette: Lois Ann Shearer was the nurse on our respiratory disease studies, and was stationed at Ord. She was Jim's right hand. Jim Chin was living there at Salinas, and Lois Ann was also living at Fort Ord on the reservation. Jack used to go down to Ord a couple of times a week to pick up the clinical specimens and bring them back here to run them through the laboratory for influenza, or for anything else we could uncover--rhinoviruses, for example. So we had a pretty good team of three people, plus me as the project leader, principal investigator, and administrative officer. Jim and I did all the planning of what we wanted to do and how to go at it.

So Jack was essentially the laboratory person, and Jim was the field person, and Lois Ann was the contact with the public. That made a very good team. Then when the Armed Forces Epidemiological Board fell apart through the intervention--which I think was self-seeking--of medical officers in the military, the team broke up. It became so difficult to work with all these activists running around the countryside screaming about civil rights and prisoners' rights and so on, that we as civilians could not function in that atmosphere.

Hughes: You mean that using recruits was questioned?

Lennette: You had to use recruits because it was a disease of recruits. The seasoned troops didn't acquire these diseases. It was the kids who came in and spent about eight or ten weeks at Fort Ord who came down with influenza, with atypical pneumonia, with these coxsackie virus infections, and we were studying influenza and adenovirus vaccines. Now influenza, like some other epidemic diseases, is erratic, unlike measles, which occurs in huge proportions about every four years; every time you accumulate enough susceptible population of young children, you'll have a big outbreak. (We don't now because we immunize them.)

This meant that Lennette's Law, "You cannot evaluate a vaccine in the absence of the disease for which it was designed," was difficult to implement. So we would inoculate ten thousand trainees during the course of the year, but influenza never showed up. So that's all your time and effort and money gone for naught. Now if influenza did occur, you had a sufficiently large immunized population to see how good that vaccine really is. So that's what we were doing.

Then came the sixties and all the social unrest and the activism and everybody screaming for his rights and the hell with everybody else. The "me generation." You know, "What's in it for me?" kind of business. Then we couldn't operate because theoretically the interpretation was that you had to get the "informed consent" of every single recruit before giving the vaccine.

Hughes: Did you get out before you were actually questioned, or was there a mandate from above?

Lennette: No, we got out because we just couldn't operate in that atmosphere. We had no rank; we were there under sufferance really, and some of the old-time military medical officers would sort of resent these civilians being underfoot. But all in all, we could see that we couldn't handle this, and there was no point in even trying, so we pulled out of it, and then the military took over.

Hughes: Did they actually take up your study?

Lennette: The study of the vaccine? Yes, but this was self-defeating, as you would expect, because the reason the commissions existed was that you had experts in whatever field it might be, and usually these were people within the university who would pursue a study for years and who had graduate students to assist them. Further, like firemen, these investigators were always "on call" and ready to study disease outbreaks anywhere in the world at an instant's notice.

##[telephone interruption]

First of all, you have people, let us say, in the university, or you had people like myself, who could study as we did at Fort Ord, for years--year after year after year after year. You had beautiful records, adequate records of background. You had the patient's history and you knew what kind of vaccines were given. You had all the serology on these people who were ill and came to the clinic or into the hospital. We had specimens for virus isolation, and sera for antibody studies. The clinical and epidemiological studies were well planned, well designed, even if I say so myself. And productive.

All right, now you turn this over to the military. First, they are on tours of duty, so that the medical officer who is there two or three years is transferred, and somebody else comes in to take his place. You have no continuity to begin with. There's nobody there long enough to do a study and then evaluate it. So a lot of the information just went down the drain, lost, and there was just no way to get it together to analyze and evaluate.

Secondly, if anything untoward developed, you always had some graduate students, or, as I did here in the lab, my colleagues, to provide support. We could have a team in twenty-four hours to do a special task. You can't do that in the military. So the Ord studies suffered that way. The commissions as we knew them just virtually don't exist today.

Harald Johnson

Lennette: We haven't mentioned Harald Johnson.\* Harald Johnson is unique. Harald Johnson joined the Rockefeller Foundation in the 1930s, was assigned to work on rabies, so he was sent to the lab in Alabama, a state with a lot of rabies. He worked in Montgomery with one of the foundation staff members, John Leach\*\* by name. Eventually Harald took over all the laboratory work and most of the field work. Very thorough, meticulous, conscientious kind of person.

Harald worked on rabies for some years, and then came down with a paralytic disease; he was really severely paralyzed, lost the use of both legs. The question arose, was this paralytic polio or was it rabies or, thirdly, was it due to what we call neuroparalytic disease consequent upon repeated inoculations of rabies vaccine prepared from central nervous system tissue, that is, was he sensitized to the tissue components, which is a known hazard. They never did sort that out.

Anyway, he was sent to Georgia Warm Springs, which was the polio rehabilitation center, and they worked him over and treated him with physical therapy. I don't know whether the foundation ever paid his bills or not. I think they probably took the attitude that it was paralytic polio he acquired, and it wasn't rabies. That was never proved.

So Harald, when he was "rehabilitated," had other chores to do. He worked in New York for a while on rabies. And then he was sent to India, and spent some time in Poona studying rabies and arthropod-borne encephalitis. About 1954 he was due for reassignment, so they sent him here to Berkeley to work with me. I was away when the Johnsons arrived by ship in San Francisco, so Mrs. Lennette met him and his family at the port. Harald was pretty severely crippled, using two canes. So he came to the laboratory--this was in 1954--to work on rabies and associated problems, and on the arthropod-borne agents. We gave him a lab in the back building at Acton Street, where the Virus Laboratory was situated at that time.

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\*Oral history interviews with Dr. Johnson, conducted by the Regional Oral History Office, are in progress.

\*\*John Leach was later assigned to the Philippines and was in Manila when the Japanese invaded these islands in 1941. He was interned, but later released for repatriation in 1943. He was among the returned captives on the MS Stockholm, which stopped in Rio de Janeiro en route to the States. I was in Rio at the time, and John was our guest for a brief visit. Imprisonment by the Japanese military had taken an obvious toll. [footnote by Dr. Lennette]

Lennette: Of course, after a while, the International Health Division staff in New York realized that he had been here six or seven or whatever years, and theoretically one tour of duty is three years, and you shouldn't stay more than two tours. Over the subsequent years, they tried to transfer him several times. But he's been here ever since 1954, because I fought to keep him here. I can remember some of the battles I had with New York and discussions about keeping him. I particularly remember one with Bob Morrison, director of the International Health Division, on Copacabana Beach in 1968 at the tropical medicine meetings. The result, Harald could stay in Berkeley for "the duration."

Hughes: Did he continue to study rabies?

Lennette: Yes. He still does. As a matter of fact, he's writing a chapter on rabies for me for a book right now. But he's the last of the old-time doctor-scientists. He's the kind of a guy that can go out in the field, see a bird and identify the bird by its common name and by its scientific name. Or he'll see a flower and he can give you the vulgar name and he can give you the scientific name. Just incredible.

He's a very good observer. And so he's done a lot of things most people wouldn't think of doing, like looking for animals-- he would dig them out of nests or burrows under the snow. In Modoc County, for example, he recovered viruses from various species of animals, including the Modoc virus isolated from mice under the snow. The Modoc virus, whose pathogenic significance for man is unknown, is an arthropod-borne virus. Anyway, he would go out on these field trips, collect all kinds of animals, parasites, mosquitoes, ticks. He did a lot of work on the arthropod-borne viruses, western equine, St. Louis, and others during his long career. He even developed an early vaccine for western equine. But you could never get him to publish anything!!

Hughes: He was too busy observing.

Lennette: Yes. Too busy observing and studying. He's a real student, in every sense of the word. A scholar. And I threatened him one time. I said, "If you don't write this up, Harald, I'm going to write it up. I'm going into your lab"--it's on the second floor down on Acton Street--"and get all your notebooks, by God, and just take them and look them over on the weekend and tear out the pages I want and write up the papers." He said, "Sure, go ahead. I don't care."

So what do you do with somebody like that? You can't win. He didn't care. He was not at all possessive about the things he had done. He was very open. A wonderful character. And a beautiful pianist.

Lennette: Hilary Koprowski, whenever he came to Berkeley, would get together with Harald--two pianists playing classical music. It's really something to hear. Harald earned his way through college and medical school playing jazz with an orchestra.

Hughes: A renaissance man.

Lennette: Yes, he's really something. And the students, of course, just love him--crazy about him--because he's so full of stories, full of anecdotes. He's lived through all this, you see, so the kids know he's just not giving them second-hand information. He's done all of this.

#### Hilary Koprowski and Subacute Sclerosing Panencephalitis

Hughes: Speaking of Koprowski, I noticed his name on a paper in 1972 on subacute sclerosing panencephalitis.\* Obviously you've been in touch since the Brazil days. Could you summarize that work?

Lennette: The people at Stanford called me one day and said that they had a patient with subacute sclerosing panencephalitis. [Dr. Lennette is referring to a different paper. See second footnote.]\*\* They had examined a biopsy of the brain. That's how the diagnosis was made. They also had electron micrographs, and saw something in these micrographs which was very reminiscent of a virus, and what did we think? So they sent the micrographs to us. Lyndon Oshiro looked at them, and sure enough, it looked like a virus. It looked like it might be rubeola, measles virus.

We had blood specimen on the patient, and also had some spinal fluid from this same patient. We ran the brain specimen, which was taken for electron microscopy, using fluorescein-labeled measles antibody, and the thing just lit up like a neon sign--rubeola virus was present! We ran the spinal fluid for antibody and found a high level of rubeola antibody; that's pretty unusual in the spinal fluid. We also found antibody in the blood, as expected.

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\*Volker ter Meulen, Michael Katz, Yonta-M. Kaekell, Guiseppe Barbanti-Brodano, Hilary Koprowski, and Edwin H. Lennette. "Subacute sclerosing panencephalitis: In-vitro characterization of viruses isolated from brain cells in culture." J. Inf. Dis. 126 (1972):11-17.

\*\*J. M. Freeman, R. L. Magoffin, E. H. Lennette, and R. M. Herndon. "Additional evidence of the relation between subacute inclusion body encephalitis and measles virus." The Lancet (1967):129-131 (July 15).

Lennette: We wrote this paper describing these findings and published it in Lancet with Magoffin, myself, J. M. Freeman, and R. M. Herndon. Freeman was a pediatric neurologist and Herndon was an electron microscopist/pediatrician. But we were beat to the gun by people from Belfast. Their paper appeared about a month before ours.

Hughes: How do you explain these simultaneous discoveries? It happens all the time.

Lennette: Yes, this happens all the time. People get the same ideas about the same time, you see. It's just coincidental.

Now over the years all of this has been lost sight of, because no graduate student reads more than about four or five years of the literature in the past, and they're always reinventing the wheel, and they forget the work that was done in Belfast, and they forget the work that was done in Berkeley. They are rediscovering it.

Anyway, there was evidence of measles virus being involved, and subsequently other patients were studied from this standpoint.

Now what you are referring to with respect to Koprowski and ter Meulen was the recovery of a parainfluenza virus from cases of subacute sclerosing panencephalitis. I think that's the one you're referring to.

Hughes: That could be.

Lennette: They had done some work on several patients in Germany. Ter Meulen spent a year in this laboratory, and went back to Germany where he became professor at the University of Wurzburg. He continued his studies on neurological diseases.

Hughes: How did Koprowski get involved?

Lennette: He gets involved in a lot of things these days. He's built up a laboratory with a fairly good-sized staff. He has a lot of drive, a lot of energy, very well read. And really brilliant. He's abrasive at times and difficult, not so much with me, but with others, his colleagues. There's no question that he is a brilliant person.

Hughes: So there was no historical reason for the tie-in with the lab? It wasn't because of your work in Brazil together?

Lennette: No. The early work that we did in Brazil, that was all published. Then he went on from there to bigger and better things on his own.

Hughes: Is he still at the Wistar Institute?

Lennette: Oh yes. They just celebrated his twenty-fifth year, I think, as director. Just last year or so.

More On Cancer Research

Hughes: I saw reference to the Moloney leukemia virus.\*

Lennette: That's the one that Natalie Cremer was working on.

Hughes: Was that a spinoff of your cancer research?

Lennette: It was just one of the viruses she was studying. There were several others that she was studying as part of the leukemia project.

Hughes: This is in the early 1960s.

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Lennette: When project site teams came out to review progress on the cancer project, the first thing that went down the drain was the veterinary program. They weren't too happy with it. That vacated one whole floor of the lab.

Hughes: Why weren't they happy with it?

Lennette: They were dissatisfied with the progress or the results, and it wasn't very imaginative or whatever. They just weren't happy, so they refused to fund it. Epidemiology then also fell apart. There wasn't enough direction. The veterinary part was doing pretty well. It was still functioning. But there were several directors of the veterinary project, and the last one who came in was having difficulties with the university and the administration, mostly our own administration here. So my advice to him was to take his staff and move up to Davis, because he worked on veterinary problems anyway. Which he did. He was given a home. So far as I know, he's still up there. And that left only the Virus Laboratory. So we gradually phased out, too, as Huebner's influence declined and we had less and less support.

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\*Natalie E. Cremer, Dee O. N. Taylor, Edwin H. Lennette, and Shirley J. Hagens. "IgM production in rats infected with Moloney leukemia virus." J. Natl. Cancer Inst. 51 (1973):905-915.

Water Virology

Lennette: We began to look at other channels. I could see the handwriting on the wall with respect to viruses and cancer. That's one of my responsibilities, to see which way the tide is flowing, or the river is going to go.

So I got John Riggs, who had been working in the cancer field, to transfer over to water virology. And John said, "Well, I don't want to work on that. I don't have any interest in that." I said, "John, this is the only way we can go. Try it. Here's a whole bunch of reprints. Take them home and read them over the next few weeks or months." Which he did.

Hughes: Now why did you think of water virology?

Lennette: I'll get to that in a moment. So I got John going on that. Well, he was lukewarm toward the whole thing. But like many other things, once you begin to do something--like, "I don't want to repair this automobile. I don't know anything about these engines." You take it apart and pretty soon you get interested in how the thing functions. John was the same way. He picked up some interest in what he was doing and eventually got very much immersed in it. And he was a natural for this, because he is a good virologist. I don't mean in a theoretical way. He's a good, basic medical virologist who knows field work. He's not afraid to go out and get himself dirty. He's not afraid to work in the rain and mud.

What had happened was, some years back, I received a telephone call from Dr. Howard Bodily, who had been the former director of the Division of Laboratories in this department. He had retired, and wanted to go on to other things, a change of pace. So he became sort of a consultant or associate of the American Public Health Association to help set up conferences and meetings and teams and so on.

He called me one day and said that the APHA had received a fifty thousand dollar grant from a commercial group which was interested in setting up a symposium on viruses in water. I said, "Howard, I don't know very much about viruses in water, but why do you want another meeting? There have been three or four of them in the last several years. There was one over in Europe, as I recall, in Scandinavia. There was another one up in the Northeast here, and there was another one somewhere else. Why do you want another one? It seems to me you're just going to have the same crowd of actors giving the same old worn-out speeches and platitudes. Why don't you do something different?"

Lennette: "Like what?" he asked.

I said, "All right. You want to have a meeting? Get fifty thousand dollars, invite some of the people who are working in the field, plus a few people from the outside, sit down and assess the state of the art. What have we done? Where are we? What are we doing?"

He thought it was a pretty good idea, so he got Joe Melnick, who had been working in water virology because he was one of the first people into the field. Joe's got his fingers in everything. He has a broad interest. He gets involved in everything. An indefatigable worker. I don't know how he does all these things. So he got Joe Melnick; Gerald Berg, who was with EPA in Cincinnati, and who was also working on viruses in water; and Ted Metcalf from the University of New Hampshire, who had been working on viruses in water and in shellfish. And myself. I didn't know anything about water supplies, except what I'd read or heard. I was the least knowledgeable of the group.

So this was the committee to set up this international conference scheduled for Mexico City. Then we all get down to Mexico City and environmental scientists are presenting papers. I sat through the first day and thought this was pretty dreadful.

The second day, I just listened with more and more disbelief, and finally had to say, "Well, I think a lot of the things we're discussing have been known for years." I'm talking here about the relationship of viral particles to what you see in microscopy, and Joseph Beard was working with chicken leukemia virus twenty-five years ago. He described the presence of the virus in chicken serum, and also described the appearance of the virus by electron microscopy, and the relation between infectivity and viral particle count. He said he didn't know why people couldn't see the viruses in chicken serum, because there were so many particles, it was a wonder the blood wasn't solid.

A lot of this information was in the medical literature, and what had happened, these people never saw it. It's another one of these recent phenomena where you organize into... We have departments of environmental science, and you'll get some microbiologist on the faculty who then is teaching microbiology of water. And then he just passes on his lack of information to the next guy, and the field becomes an incestuous relationship. It's a continuous passage of either misinformation or lack of information. And there's a lot of medical literature which doesn't appear in the environmental journals or in the engineering journals.

Lennette: So here I was from the outside, knowing nothing about water virology, and I was making all these critical comments. Well, it kind of shook the meeting up a bit. But I now became an expert. Three months later I was invited to participate in a meeting in Boulder, Colorado, where they were talking about sludge and so on. Then another meeting in New Hampshire. There were three or four of those, which made me an authority on viruses in drinking water and in waste!

After I got around to the second or third one of these meetings, I became interested in what these fellows were talking about. I didn't agree with everything that was being done, but I could see what the problems were and how they should be attacked. But nobody was doing anything much about it. And that's why I got John interested.

He's just put together a paper, and he's got a second coming out, on Giardia lamblia. Giardia is a very small parasite which first came into prominence in this latter day age in the Soviet Union when one of our American missions, composed of people from the Center for Disease Control, was in Leningrad, and came down with giardiasis. The parasite was present in the water supply. Well, we have since found that ordinary chlorination doesn't kill off these parasites. But how do you find them? How do you test for them? John has developed a method of concentrating the water and getting the giardia out and staining them by fluorescent antibody. Beautiful technique. It's a real advance. So now this is going to create problems for the water works. They can find these things in their test samples, but how do you get them out? So that's how he got interested in it.

#### Cytomegalovirus (continued)

Hughes: We talked about cytomegalovirus, but do you want to say something in a summarizing way?

Lennette: When I was a young instructor at Washington University in St. Louis--this is back in 1938-39--Margaret Smith was working in this field. At that time cytomegalovirus was called submaxillary gland virus, and was found in mice and in guinea pigs. She was studying this virus because it's easy to study a virus in a natural host. And then when the NIH study sections came in as a research funding mechanism, she continued to be funded to study animal CMV because of the possible relationship with cytomegalovirus in man. And then later it was found that these viruses were all in the same family.

Lennette: Eventually her funds were cut off because people in subsequent years just couldn't see what relevance this had to human medicine. Another one of these farsighted observations by the establishment! It developed later on that cytomegalovirus is a very ubiquitous infection. It infects a lot of people. It contributes a great deal to the pool of mental retardation. How much it contributes we don't know, but we know it's an appreciable amount. And also to congenital defects. So looking for cytomegalovirus today has gotten to be a real routine procedure. You look for it in the mothers or in the children. The tests are very simple. So here again, because you're looking for the presence of a virus which is almost ubiquitous, and it infects everybody sooner or later, you've got a great commercial market for diagnostic materials.

[telephone interruption]##

It's virtually an ubiquitous infection and one that has to be seriously looked at, so that if the mother has it early, what are you going to do about the fetus? This sort of thing. These are all medical decisions. But more and more testing is being done for cytomegalovirus, to the point where now the manufacturers are producing kits. The old kits, which used to be called Torch, which stands for toxoplasma, rubella, cytomegalovirus, herpes, were not very good, but the new kits that are coming out are quite good, and they're being widely used now.

Hughes: And what was this lab's contribution?

Lennette: We helped to work out some radioimmunofluorescence techniques.\* Of course it's easy to diagnose because you just centrifuge the virus-containing cells out of the urine, for example, and then stain the cells to reveal the virus.

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\*James D. Kettering, Nathalie J. Schmidt, Dana Gallo, and Edwin H. Lennette. "Anti-complement immunofluorescent test for antibodies to human cytomegalovirus." J. Clin. Microbiol. 6 (1977):627-632.

Varicella

- Hughes: How about varicella? I don't have a date for those papers, but I know that Weller had reported problems with actually unsticking the virus from the host cell.
- Lennette: The virus grows very slowly in the cell, and it's what we call "cell associated." It's hard to separate it from the cell. So Nathalie Schmidt devised a number of methods for getting the virus out, including the use of buffers. Her interest, however, lay more in simian varicella viruses that occur in chimps. She's done a fair amount of work on that. There's one simian virus, for example, called the delta virus, that was recovered from simians in the Delta Primate Regional Center in New Orleans. She's done a lot of comparisons of those viruses with human strains, and they're closely related.
- Hughes: Are there any other strands in the line of research that should be mentioned?
- Lennette: No, I'll probably think of them an hour after the meeting, or at three o'clock in the morning when I usually wake up. I could get my pencil and write it down.
- Hughes: The way I culled these topics was simply by going through the bibliography, and anything that had been written about several times I wrote down. So I hope I've gotten all the major research areas.

Editorial Efforts (continued)

[Interview 7: February 3, 1983]##

- Hughes: In 1970 the first edition of The Manual of Clinical Microbiology was published, and you and John [E.] Blair and Joseph [P.] Truant were editors. I was wondering how the manual came about and why you three became editors.
- Lennette: John Blair was the chief of microbiology at the Roosevelt Hospital in New York City, and a consultant in microbiology, Hospital for Joint Diseases and Medical Center in New York. He was widely recognized as a very capable clinical microbiologist/bacteriologist. Joseph Truant was the chief of a clinical bacteriology laboratory in Michigan at Southfield, just outside of Detroit, and was also on the staff of Providence Hospital there. He eventually developed a consulting service of his own, as well as running a laboratory of his own, and is now on the staff of the Advance Medical and Research Center at Pontiac, Michigan.

Lennette: The first book was rather small, seven hundred pages, and seemed to fill a real need. In the interim John Blair died, and this left Truant and myself as editors. In 1974, we brought out the second edition with the assistance of Earl Spaulding, who was chairman and professor of microbiology at Temple University in Philadelphia. The fifth edition, with myself still as editor-in-chief, came out in 1985, and with fourteen hundred pages, is twice the size of the first edition. My associate editors were Albert Balows, William J. Hansler, Jr., and H. Jean Shadomy.

The reason I was included in the editorship was the clinical virology aspects, which were then beginning to show some importance in microbiology. Since I was operating for some years in a clinical and public health virological ambiance in Berkeley, the American Society for Microbiology, publishers of the Manual, felt I would be the logical person to contribute to the book, or to try to edit it. So that second edition came out as Lennette, Spaulding and Truant, not necessarily in the order of importance, but alphabetically.

Hughes: Why do you say that virology was coming to be important to microbiology only in 1970?

Lennette: You see, virology was not much of a field, really, until in the fifties some laboratories showed a desire to do clinical virology work. But they were always stymied, always held back, by the fact that reagents were not available. So it was only a large laboratory, such as this one, which had sufficient staff and sufficient monetary resource to make its own antigens, that could function. It was a catch-22 situation. The manufacturers, whom I tried to interest over nearly forty years' time to make antigens and antisera and other reagents, just weren't interested. They claimed there was no demand, although I repeatedly pointed out that, "There's no demand because you're not creating one."

In the sixties there still wasn't an awful lot of clinical virology being done. It was towards the end of that era--about 1965 or thereabouts--molecular biology and specifically molecular virology began to open up and to give us leads and a lot of tools to attack some of these problems of disease. Therefore, there was more interest in clinical virology, so that we included some virology in that second edition, which brought me in as the editor-in-chief.

The other thing, it's the usual story: If you want something done, and you want some suggestion that it might be supported or successful, find the busiest person you can. [laughter] So this is why they approached me to be the editor.

Hughes: Are you saying that it was the first time that virology had been included in a text or a manual of clinical microbiology?

Lennette: So far as I know. It might have been in some of the European books, but there was nothing that was really reliable and helpful and worthwhile in the U.S., so far as I can recall. Now there were texts appearing on virology, but these were more basic virology. A great portion of the texts, for example, would be concerned with bacteriophage. Of course the information there was not virology in the sense that you could use it in the hospital or for other things, but virology in the sense that it gave birth to molecular biology. If you really want to speak broadly, virology is the foundation on which much of molecular biology is built.

Hughes: And that's the sort of virology that is common to an academic atmosphere, is it not?

Lennette: Yes. When you come right down to the clinical part, the books, the texts, for clinical laboratory virology were written in this department by Nathalie Schmidt and myself. We didn't do the writing. We did the editing. We contributed our own information. But we got together a group of authors, a group of contributors, who were specialists in various fields of viral diseases--some were working on herpes, some were working on polio, some on the enteroviruses. We got them to write a chapter in the book. Not in the Manual of Clinical Micro now, this was just the beginning. I'll refer to that in a moment.

Under the sponsorship of the American Public Health Association, Nathalie Schmidt and I put together several editions of a book called Diagnostic Procedures for Viral and Rickettsial Infections. The first two editions were put together by Dr. Joseph Smadel, who was the director of the Walter Reed Hospital Virus Laboratory, and by Dr. Thomas Francis, Jr., of influenza fame, who at that time was professor of epidemiology at the University of Michigan School of Public Health at Ann Arbor. The Committee on Laboratory Standards and Practices of the American Public Health Association felt that it was time to bring out a book on diagnostic virology. The first two editions that came out were rather skimpy in content and in pages. I don't have the copies here in the office. They're at home in my historical collection. They were rather small, maybe a hundred or so pages, because there wasn't too much known.

Lennette: And then for the third edition\* I was asked to take over. Smadel and Francis had other fish to fry, and they felt that they had done their stint as editors; maybe someone else should take over. Since I was running a rather large operation here from the diagnostic standpoint, although it was mostly public health virology, not clinical virology, they felt maybe I would be a logical candidate to put together future editions. So I discussed it with Nathalie Schmidt, who is my colleague and was my right-hand person at that time when we started the laboratory, although she is an independent investigator. She and I agreed to do it. So we put through the third edition. A lot of pains and a lot of troubles taken to make it as good as we could. And it was an instant success.

This was followed by the fourth edition in 1969, and the fifth edition came out in 1979. It's a book of about eleven hundred pages, and it's a scholarly work; covers important viral diseases of man in considerable depth and detail. It is, you might say, the bible for the clinical virologist all over the world. Unfortunately, the American Public Health Association's marketing efforts were so poor that the book never really got the distribution that it deserved or needed. No commercial publisher would ever think of doing the things that were done by the American Public Health Association, either through naivete or lack of funds. I don't know which. Perhaps both.

Hughes: How does Diagnostic Procedures compare with the manual?

Lennette: The manual, for the second edition we put in some virology. But the virology section is only part of the book. It's a small section, maybe two hundred or three hundred pages. That is geared more to people whose background and interest is primarily in bacteriology and parasitology, but have to know something about virology. So this is sort of a cursory overview. It does contain information on how to do tests. But this is not the book that a full-time, professional virologist would use at the bench; Diagnostic Procedures fulfills that. Diagnostic Procedures for Viral and Rickettsial and Chlamydial Infections\* still leaves a gap, because that's a scholarly book, and many people just don't find all that detailed information useful to them.

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\*Edwin H. Lennette and Nathalie J. Schmidt, eds. Diagnostic Procedures for Viral and Rickettsial Infections. 3rd ed. New York: American Public Health Association, Inc., 1964.

Lennette: So somewhere in between there ought to be a book, which I'm working on now, that would appeal to the people in between, that would have something for the bench worker, the laboratory technologist who is trying to do tests, and the supervisor in the laboratory, who is generally at the doctoral level, M.D., Ph.D., D.V.M., Sc.D., whatever, and something out of which the clinician can get something, so that he knows what the basis is for the tests.\*

We're not trying to make this into a book that's devoted to infectious diseases. The main purpose is to present enough of epidemiology and immunology and pathogenesis that the individual using the book and doing the tests will have some concept of what the underlying structure is that permits you to do this kind of a test. So it's a different kind of a cat.

Hughes: With whom are you working on this?

Lennette: I'm doing the editing myself. I'm doing this for Marcel Dekker, which is a private publisher. They publish a lot of medical books here and in Europe.

Hughes: But you'll be the sole editor?

Lennette: Yes.

This Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections may go through another edition. We're already talking about another edition of the Manual of Clinical Microbiology. Both books are up for reexamination and incorporation of criticisms made in the past to fill in any gaps that might have occurred. So the two new books that come out may be quite different. And we may even drop out the virology from the Manual of Clinical Microbiology and make a companion volume on virology. There's a companion volume to this book Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections called Diagnostic Procedures for Bacterial, Mycotic and Parasitic Infections.

Hughes: You have your work cut out for you, I would say.

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\*Edwin H. Lennette, ed. Laboratory Diagnosis of Viral Infections. New York: Marcel Dekker, Inc., 1985.

Lennette: I feel somebody has to do this. It's a terrible chore. You try to get forty or fifty authors that you're working with all lined up, and keep prodding to be sure that they're writing their chapters so that you can meet your deadline. After all, there are deadlines. Manufacturing deadlines. Redactory deadlines. You have got to keep after people. There are more interesting things that they want to do in the laboratory than write chapters. They always leave these writing commitments to the last moment. As you know, the road to hell is paved with good intentions, and people always intend to do everything, and at the last minute they find out that they haven't.

Also, it's a horrendous task if you're dealing with thirty chapters, and they're all dumped on you at one time, and you're trying to read and edit them. You do have to have uniformity of presentation. Your terms have to be the same. You can't use different terms in different chapters. You can't use different abbreviations, different acronyms. Responsibility for consistency in use of such items falls on the editor.

Hughes: What about standardization of methodology? What if one laboratory has a slightly different method than another?

Lennette: I tried repeatedly years ago to get people to standardize methods, but never got very far. Every scientist has his own way of doing a procedure or test, and his way is the best, obviously. So what I do is try to get these laboratory scientists to say, "There are three or four tests which are useful, but in our laboratory we prefer this one," for whatever reason, and let it go at that. But do give the reader information, should he decide he wants to do something else. There's no uniformity on these tests in general. That will come with time. But originally there weren't enough people working in the field to get together. Nor was there the huge commercial stake that is now involved. Huge is relative. It's not big compared to chemicals.

Hughes: You're thinking now of the backup materials?

Lennette: I'm thinking of people who prepare diagnostic kits for virology. People like Abbott Laboratories, Dynatech and Immulok, and some of the others who produce kits. There's a large commercial volume for these kits because they're dealing with diseases in which there is a great interest because of high morbidity. So if you're going to produce a kit, you've got a lot of competition with others who are also in the business, like these herpes kits. Everybody is competing with everybody else to produce the herpes virus diagnostic kit, so you've got to produce a good product, and then you standardize the tests.

Lennette: Even that has not been completely worked out, because some of these tests depend on instruments for reading, and manufacturers are devising their own instruments to read the tests done by their own procedure. So if you have six different viruses with six different procedures and six different kinds of instruments, nobody can afford that, not even a large laboratory. We're talking about instruments that cost several thousand dollars.

So standardization is coming, but it's coming pretty much on its own, hit and miss.

#### More on Viral Diagnosis

Hughes: In the old days, before there was such an armamentarium, what would happen if there was an outbreak of a viral disease, and the public health lab involved in that particular area just didn't have the methodology worked out? Would the samples be sent out of state?

Lennette: In the early days there were no viral diagnostic laboratories. This one was initiated back in--1944 really is when we began to do diagnostic work. The laboratory was here several years before that, but anything diagnostic was purely incidental to the research program that was being carried on by Monroe Eaton. He was working on respiratory disease. So as a byproduct of having to examine these materials in the lab to be sure what the diagnosis was in these patients, he did the tests, mostly for influenza, and later on for atypical pneumonia.

Hughes: He wasn't getting much material from out of state?

Lennette: No, he was getting it purely locally here in the Bay Area. And then when I came in, I saw the possibilities of this laboratory. Now mind you, my interest was always not in basic, fundamental virology; it was in applied, medical, clinical virology and public health--public health mostly from the epidemiological standpoint. So this laboratory, like the laboratories in other health departments, was not geared to taking care of the patient in the hospital, but to determining what's happening in the community or in the region or the state.

For example, whenever influenza appeared, this laboratory would know two or three weeks ahead of all of the physicians, even on the reporting end, that influenza was building up or that it was rampant. By the time the doctors sent in their reports to the infectious disease officer of the health department, they had already sent blood specimens to us and gotten

Lennette: the diagnosis. Then they sent in their reports to the infectious disease section. So the laboratory in general was the first to know of any outbreaks--measles, mumps, anything else that was occurring.

But we were not geared to providing a diagnosis that the physician wanted for one of his patients. We were a public health laboratory, and we were studying disease as it hit the whole community, not the individual, to follow its epidemiology. And that's a different kind of a need. I tried to resolve that by getting hospitals interested in sending material to us on patients. We could just never get it off the ground.

Hughes: What was the stumbling block?

Lennette: Well, getting the specimens in in a timely fashion was one. There was no courier service that could get the materials to us promptly. We didn't have a staff that was geared that way. We're talking about 1940s, early fifties. And then we didn't have all the rapid diagnostic techniques either that we have today.

But today you could gear the laboratory to diagnosis in a given individual. With all the new developments of immunofluorescence and immunoenzymatic methods of approaching disease problems, radioimmunoassays, we can get the answer out in a matter of hours or a few days, rather than a couple of weeks. And these long delays associated with laboratories such as our own, to be frank, gave rise to the attitude, "Why bother sending anything to the Virus Laboratory? By the time you get an answer, the patient has either recovered or he's died. So it's pointless."

Hughes: So the physician fell back on clinical symptoms?

Lennette: Sure, he used his own acumen. That's the way medicine really should be practiced. You should use your God-given senses to make the diagnosis.

Hughes: In many things, that works pretty well, but I would imagine some of these more exotic viral diseases would throw the everyday G.P. [general practitioner]

Lennette: That's true. You have to look at these things historically, because in the old days the medical officer of health, as they call them in Britain, was always an individual trained in infectious disease, so if you as the local parish physician made a diagnosis of smallpox or chicken pox, that case had to be seen by the medical officer of health, who made the final diagnosis because he was an expert. The public health officer today is a pencil-pushing bureaucrat. He doesn't see any patients, and he's the last guy you want to talk to, speaking in generalities, about clinical diagnoses.

Lennette: So you do have to have these tests. Some of these students today have never seen a case of smallpox, have never seen a case of polio. Late fifties is when we conquered polio, and they don't know anything about the old days when the hospital wards were filled with paralytics, and we had beds out in the hallways, and respirators going by the dozens. They have forgotten those days. So you do have to have a test which will discriminate between conditions which are hard to differentiate merely by looking at the patient. By this means, you find that there are a lot of diseases occurring which we didn't know about originally, such as some of the arbovirus infections. The importance of other diseases, like cytomegalovirus, over the years has been worked out and found to be very much more important than originally suspected. Well, we suspected that it was because of its contributions to mental retardation, but we never knew how important it was until recently. Even so, the epidemiology and natural history of the disease contains large hiatuses of ignorance.

Hughes: So the techniques brought all these new diseases forward.

Lennette: Yes. They gave us the tools and methods to discover these new diseases and to increase our knowledge of old ones. You still have good examples of this dichotomy, of this anachronistic situation, because the State Department of Public Health laboratory division here deals with the epidemiology of disease. This laboratory exists, really, to give support to the epidemiologist; the infectious disease people on the staff here study epidemics. Their results frequently are delayed because of the nature of the operation. Now laboratories are springing up which can use these modern techniques for diagnosis, and they are commercial laboratories.

Hughes: A few minutes back you used the term public health virology. Is that differentiated from epidemiological virology?

Lennette: I speak of public health virology because of the materials that doctors sent in to us. They were interested in what their patient might have. And the best we could do was to say, "Well, last week we had X number of cases; this week we've got X+1; and next week we've got X+2. The curve is going up."

And then we would warn our infectious disease people, "There seems to be a lot of flu around here." Or conversely, "There's a great deal of respiratory disease around--they're sending material--but it isn't influenza." We didn't know what it was. Now of course, some of these we could sort out. That's public health virology.

Lennette: Clinical virology is when a specimen is gotten from a child at Children's Hospital, sent to the laboratory by courier, and the test is run that afternoon, and the doctor's got the answer by five o'clock, or by nine o'clock the next morning. That's clinical virology. That's what it should be.

Hughes: And epidemiological virology is on yet a broader scale?

Lennette: It's even broader because you've got an epidemic of something in the community. Or there's something occurring. Doctors call in and say, "We are seeing a lot of respiratory disease," or, "We are seeing a lot of people with muscle pains." Our people go out into the field and see these patients, examine them, get some idea of what it is clinically, come back with specimens, which may be stools or urines or throatwashings or blood. These then are run in the laboratory to find out what the cause of this outbreak is. That's how we picked up foot and mouth disease here in man, by that kind of a tactic.

Hughes: Then the doctor in the street, to coin a phrase, is likely to call in the public health department when he gets a run of patients with a certain disease?

Lennette: Yes.

Hughes: That's something that the average doctor would think to do?

Lennette: I won't say the average doctor. Some of the better practitioners in the area. The average doctor is too busy to take the time. He's got an awful lot on his mind. Unless he's scientifically oriented, or he has a real interest in infectious disease, he wouldn't. Of course, some diseases he has to report by law.

### Laboratory Funding

Hughes: A very broad question: How was and is the laboratory funded?

#### The Rockefeller Foundation

Lennette: Well, the laboratory funding originally came from the Rockefeller Foundation. It came out of the budget of the International Health Division of the Rockefeller Foundation. So all of Dr. Eaton's money, the operation of the lab, salaries and so on--as a matter of fact, even most of that building at Acton Street--was put up by the Rockefeller Foundation. That ran for some years.

Lennette: I was brought up from Brazil and assigned to Berkeley. My salary was paid by the foundation. But the original compact made between the State of California and Dr. Sawyer, the director of the International Health Division, was that as viral diagnostic tests are developed, we, the Rockefeller Foundation, will retreat and will turn all of the operation over to the State. Which means that the State then would operate the laboratory, pay the salaries, buy the equipment, do the testing and reporting, and so on. That came around 1952, as I recall, when the State took over the whole operation, paid all the salaries. The building was deeded to the state.

#### The State of California

Hughes: By what criteria was it judged that it was now time for the state to take over?

Lennette: Eaton had been here since about 1938, when the laboratory opened, and I came here in 1944. He was working on primary atypical pneumonia. Doing a very fine job of working out the disease, he and Dr. Gordon Meiklejohn, his associate.

I had been sent here to work on hepatitis, which in my estimate was a futile assignment, because I didn't see that I could get anything out of the hepatitis field. Nobody else ever had, and I could just see I was coming to the peak of my scientific career, and I was just going to waste two years of my time. So I requested permission to work on some other things. They said, "Sure, work on the encephalitides if you want. Western equine, St. Louis..." Which I did. This is 1944 now.

Over the next six years or so, the hemagglutination inhibition test was being worked out for viruses other than influenza. Complement fixation tests were also. And I, in conjunction with the people in the New York office, felt that the laboratory ought to really devote its efforts primarily to diagnostic work, and secondarily to basic or developmental research. But primarily to development of diagnostic tests. We've got certain tests now; can we make them simpler? We don't know anything about how we should collect specimens, how we should handle them, how we should process them. That became a whole area for inquiry.

Lennette: As I think I told you earlier on, we got started in 1946, '47 and '48, to do these tests. We had to just give up and throw out all of the books on virology, because these were books written by academic people who dealt with viruses that had been grown and cultivated in their laboratories, that is, under unnatural conditions.

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In consequence, the American Public Health Association brought about the first editions of Diagnostic Procedures for Viral and Rickettsial Disease. Laboratories were beginning to realize that the viruses coming fresh from the animal host--it could be a veterinary problem, too--were quite different from the same virus repeatedly passaged in the lab. And we could no longer depend on a research laboratory to test specimens for the physician. This ought to be an operation carried out in its own right and recognized as being a diagnostic operation. Nothing fancy about research or anything else; We're here to test this specimen and give you an answer. That was the philosophy.

Then over the years, as we develop better and simpler tests, we will get out of the business. We will just close up the laboratory as primarily a diagnostic lab, and use it for teaching, research, and support for field studies.

Now this was my philosophy. The foundation agreed with me, and so did the state, insofar as they knew what I was trying to do. Public health at that time was a small department. It was not, as it is today, just the mere tuft on the dog's tail, the dog being MediCal and social welfare programs. It was our philosophy that we would try to get testing down to the local levels. We felt there was no greater advantage for somebody in Ventura sending a specimen all the way up to Berkeley when you could have a local laboratory test it there. You don't have to go through all this business of mailing things and losing them, or whatever, and you get an answer faster.

We felt, oh, about ten years ago, that we had reached that stage pretty much. So Dr. Magoffin, who was on the staff at that time, sort of my alter ego--we tried to persuade the local health officers to take over these operations. It was virtually impossible for them to get this put into their budget, because whenever there was any money available, they preferred to put it into nursing or health education or social welfare or whatever it was. The laboratory was always at the bottom of the totem pole.

Till about five years ago or so--six or seven years, maybe--we decided this was it, and we just sent out an ultimatum: We ain't gonna do no more testing for nobody nohow. That kind of shook the tree a little bit, and some of the laboratories have put up their own labs.

Lennette: Insofar as the larger health departments are concerned, they're doing all right. They can't offer the whole variety of tests that a big regional lab can, but they're doing quite well. It's only the smaller ones who can't survive if they have to have the kind of budget that's required. Well, a one-man or two-man laboratory just can't do this sort of thing. You've got to have a larger staff, like San Francisco or San Diego or Los Angeles County. You can't do this up in Del Norte.

Hughes: So the small labs send their material out.

Lennette: The small labs have to send their material out, use a commercial laboratory, or send it here. This is now recognized; it's a fait accompli. So you say, "Well, I don't see that the laboratory doors have been locked and everybody has left." No, they have not. For one very simple reason, that is, training and research.

My philosophy was that I did not want a whole staff of technicians or technologists, all of them highly expert in one specific task in the laboratory. I didn't want one individual to inoculate only mice and another one to inoculate only embryonated eggs and the third one to do only serology and a fourth one to do only tissue culture and a fifth one to do only virus identification. I wanted every person on the staff-- at that time they were mostly women; the economics of laboratory medicine have shifted considerably since then--to rotate through the lab sections and know how to do everything.

This wasn't really largesse on my part. It wasn't that I was so beneficent. It's just that I was protecting myself, because if we ever had a big epidemic of something, I could assign my whole crew to work on that, and I wouldn't be caught short. Well, as influenza came along, we would assign two or three additional people, depending upon the workload. In the summertime we might have a large series of specimens coming in dealing with encephalitis out of the Central Valley. If the workload was too large, we put some more people on. You plugged the holes wherever they occurred with a staff that was highly competent.

Now all of this took place during the days of Earl Warren's governorship. He was very health minded. He gave us a lot of support. And for the many early years the laboratory was growing, he gave us full support. He gave us what we needed and built this into what became, if I may be so immodest, the finest diagnostic laboratory in the country. And I think it still is. But there was no question. It was well equipped. It was well staffed. And it was a leader. It was highly respected.

Lennette: With succeeding administrations, emphasis began to go elsewhere, and with successive cuts in budgets and in staff, we lost this ability to circulate people. In order to do that, you've got to have two or three extra positions on the staff, so that you have some relief. We lost all that latitude. So today we can't do that, which I think is too bad.

But how do you convince a layman? That's part of our big problem, you see. We have a whole big department up in Sacramento filled with bureaucrats and administrators. We're administered and we're bureaucrated to death by people who don't know anything, and some of them down right stupid, who tell you how to run a laboratory. If they know that one exists! Because most of them don't. They don't have any perception of what's going on in Berkeley. They are always amazed when somebody goes up to Sacramento and tells them what's been going on here. What kind of a staff we have. And they put together expert committees or advisory committees, and scientific situations, and almost invariably there's nobody on the scientific staff of this department who serves on that committee, because they don't know we exist. And if they do know, they don't think we're as smart as the people from out of state.

You know the old definition of a consultant, don't you?

Hughes: No.

Lennette: It's just some idiot with slides away from home. [laughter]

Hughes: What avenues have you used to attempt to get your needs known to Sacramento?

Lennette: We have prepared budgets, only to have them cut down by somebody who really doesn't know what he's doing. If you send up a budget at budget time, the word comes from the governor's office or the department of finance, "You can only have so much money. You've got to cut out X number of dollars. The simplest thing is not to go through the whole budget item by item. Let's look at a big item. Let's just cut out this electron microscope. That's a hundred and eighty thousand dollars. Bang! We don't have to worry about three hundred and seventy-five smaller items." That's the path of least resistance.

So this is how the laboratories--I'm not just talking about the Virus Lab, but the other laboratories, too--have suffered. Now mind you, we have some very talented people in this department, in the laboratory services branch. We have some of the leading people in air and industrial hygiene, recognized worldwide. We have one of the finest air and water sanitation groups. They've written books, edited books. They're virtually unknown in Sacramento. And these are internationally renowned scientists. It's like Cinderella.

## The National Institutes of Health

Lennette: We have to look for money elsewhere. How do you get money elsewhere? Usually from the National Institutes of Health. James Shannon came to the National Institutes of Health as director right after the war, '55 or '56, in there somewhere. He had been with Squibb Institute as a researcher working on malaria. Very familiar with research problems, public health problems.

One of the things that Shannon and his aides envisioned was to have a program that would support teaching and research. He thought research needed support, because this country was in a state of flux. Mr. Roosevelt had come into office in 1933 to redistribute the wealth of the country, I guess, and he began to tax the business people and the philanthropists to the point where philanthropy practically couldn't keep up. So the government would then take over what philanthropy couldn't do. We will support research, and we will issue fellowships, and we will support predoctoral candidates.

It sounded good. So that's exactly what happened. It built up slowly. In 1948 NIH started these so-called study sections, of which you have heard. And one of the very first was in bacteriology and virology. The first chairman of that study section, which had about ten or twelve members, was John Paul, a pediatrician from Yale University Medical School who had also been doing a great deal of work on poliomyelitis. He was part of the team of [James] Trask and Paul. Trask was also a pediatrician. And with Trask's death, John Paul took over and continued the work on poliomyelitis and turned out some very fine disciples.

John found this to be quite a chore to take bacteriology and immunology and virology all together in one study section. So I was asked to serve as a cochairman. And then the following year, 1950, John withdrew and I became chairman of the study section. So I go back a long ways. I've seen all of NIH develop.

We started out with a very small budget. The viral, rickettsial and bacteriological study section had a hundred thousand dollars for the whole year. That went a long way, because there weren't too many people in the field doing research. There were other study sections in pathology and medicine and heart and so on. From these small beginnings the institutes were built up into probably the most prestigious research institution in the world.

Lennette: Prior to the war, in the thirties when Mr. Roosevelt was taxing and spending, taxing and spending, the most prestigious institution for research in the United States, internationally recognized, was the Rockefeller Institute for Medical Research. Its first director was Simon Flexner, who served as director for many years. The support money came from the Rockefeller family. At 66th and York Avenue in New York City, there's an area of several blocks that is covered by Rockefeller Institute buildings. There was a hospital there, too, to study patients with these various diseases, and that's just across 68th Street from what is now Cornell Medical School, and across York Avenue from the Sloan-Kettering Hospital.

This, in a way, served as a pattern for the National Institutes of Health, because you had people doing very basic research; you had people doing clinical research, and you had people using a hospital to bring in patients with diseases that they wanted to study, which is just what NIH has done, but on a much larger scale. After World War II, the Rockefeller Institute became the Rockefeller University.

What happened after the war, as I said, the philanthropists were shackled. They didn't have the funds to advance. So the Rockefeller University found itself in dire straits, because it didn't have the money nor the endowments that it had before the war. They, like the rest of the university structure, had to seek assistance and funds from the Public Health Service. So their money, too, a great deal of it, comes from the National Institutes of Health, the National Science Foundation, the EPA [Environmental Protection Agency], I guess, and elsewhere. And, and as I just said, they eventually turned it into a university, so-called Rockefeller University, which in my estimate was a mistake and still is a mistake. We had plenty of good universities around. We didn't need another one. What we needed was an institution such as the Rockefeller Institute for Medical Research, which was unique, had something of its own, had its own personality, its own flavor. And now it's just another university lost in the shuffle.

So their funds come from the Public Health Service, which has huge appropriations. Well, over the years, categorical institutes were set up. One for heart, another one for lung diseases, another the cancer institute, dental institutes. Mostly, as rumor has it, it's because congressmen were afraid of all the diseases that would strike them down, most of them being so elderly.

Lennette: But then it turned out, because cancer is such a problem in the older age groups into which congressmen and senators fall, for a long time the National Cancer Institute was the pet and had huge budgets. Sometimes too large because Congress gave them more than they had originally asked for. You know, "You're doing a good job; you can use more money. Here, take some more money." And the National Cancer Institute staff couldn't use the money, so they doled it out to other ancillary projects in the other institutes. For example, Dr. Huebner. He was working on adenoviruses and their association with cancer. He was in the National Institute of Allergy and Infectious Disease. But most of his work, and later all of it, was supported by money from the cancer institute. So the largesse was distributed.

I think, despite all the criticisms which have arisen about how the National Institutes of Health operated, and still do, they've done a very remarkable job. I don't think they deserve a lot of the criticisms and brickbats that have been thrown at them. I think most of the world will concede that they have done a very good job.

Hughes: Is that where most of your federal money has come from?

Lennette: Virtually all of my money--I say my money because I was the fund raiser. Everybody else was here having fun and doing his own job in the laboratory. I was the one who had to run around and be the expeditor. Like the guy who runs around for the circus, puts up all the posters two towns ahead. That was me. So I worked with the NIH people early on. As a matter of fact, our first grant came from the Center for Disease Control. It was a small amount of money, maybe ten thousand dollars, to work on Q fever.

And then from that we built. We got money from the Armed Forces Epidemiological Board to work on influenza vaccines and respiratory diseases. We got money from NIH to work on mumps. Some work on herpes and some of the other viruses. Mostly epidemiological studies. We got some money from the Rockefeller Foundation to support fieldwork on the encephalitides, mostly Harald Johnson's work. So our support came from a variety of sources.

Hughes: Was the state money mainly going into supporting the plant itself?

Lennette: The state money supported the laboratory operation, and the diagnostic end of the laboratory. It supported most of the technical staff, my salary, Dr. Magoffin's--Dr. Schmidt's salary came later; supported quite a bit of the technical staff, all the utilities, and paid for much of the expendible supplies, glassware and so on, chemicals, reagents, and for a fair amount of equipment. And the rest, the big research money, came from outside sources.

Lennette: Now that is not unique, because the University of California had the same problem. They had to have a certain basic funding of their own to support the teaching load, and the story I used to get was that maybe five percent of the university budget went into research. The other ninety-five percent came from outside agencies. I was amazed when people told me that.

Hughes: Do you think that federal grants were awarded as readily to a public health lab as to a university lab?

Lennette: No, they were not. When I came here, I knew what I was doing. I didn't walk into any of this blindly. I saw an opportunity in California where you could do epidemiology--that's what I was interested in. I could get a clinical appointment and a teaching appointment. Dr. Malcolm Merrill arranged for me to have a teaching appointment across the street in the School of Public Health, which made up some of the salary difference, because I came here at a considerably lesser salary than I was getting back East.

I saw the opportunity here to work on Q fever, which I was greatly interested in. I felt every health officer was an agent, one who could get study material for you. We'll have all the material we need. If we go out to work in the field, he can clear the path for us. That was one thing. Secondly, I could have my own show, and I wouldn't have to worry about teaching, although I was doing some across the street. But my career didn't depend on teaching. These sorts of factors.

So when I arrived here, I knew full well that we would have to make good, because the reputation of health department laboratories as concerns research was very, very poor. The general consensus was, by most people in academia and even in industry, that state health department staffs were people who couldn't make it elsewhere, and they were not the very best that you could get. They were hacks, laboratory hacks, with no imagination, no nothing. When I came here, I was aware of that, although that was not true of the California department, because they had a good laboratory service. Their people in bacteriology were very well known all over; they were outstanding. The same was true of New York, which also was exceptional.

We had to prove ourselves when we started asking for grants. "Why should we give money to a public health laboratory in Berkeley when we could use this in Berkeley across the street at the university? We've got some good scientists there. We don't need these nonentities in the health department. And we've got good people at the University of Pennsylvania. We've got good people in New York. Why give it to public health?" So we had to prove ourselves.

Lennette: As I have so often remarked when I've been asked this question which you just asked me, that everything being equal, we wouldn't have had as difficult a time as we did to establish the reputation that we did had we been across the street in the university. You can get a lot of inept people on the faculties across the street at the university. You can get downright incompetent people. You can get people who have already retired when they get on the faculty, and they ride on the reputation of the university as a whole, which has been established by people like the Nobel laureates and so on. In other words, they have an aura about them, so that if you happen to have an appointment within the university, whatever it might be, Cal or Stanford or Harvard, you immediately are annointed with something special. "Look at me. I'm from X university as a scientist." Whereas that sort of a situation doesn't accrue to people in a health department. Or in industry. These are people who are accused of--they don't have any imagination. They're not very intelligent. They don't know how to do science. Therefore they end up as second- and third-raters in some backwater institution like a health department.

We had to overcome that. So within a matter of a few years, because of people that we attracted to the staff here, we were looked upon with respect. And we have respect everywhere today. You mention the California State Department of Health, it's still well known. We lost that reputation as an entity; the health department, which used to be number one, along with New York, in the United States, now is probably about number five if not number ten. Except for the laboratory services branch.

Hughes: Is that again Sacramento's fault?

Lennette: Yes, Sacramento. Our political seers, our political powers in Sacramento, can be thanked for that. They've destroyed this department, despite a lot of protestation. But the laboratories are still respected, and they're very highly regarded.

I can't talk too much about the other laboratories, but anywhere you go in the world, you talk about this laboratory, the Viral and Rickettsial Disease Laboratory, you'll find people who are graduates of this laboratory, who have been here, who have worked here, who know about it, and whose superiors in the health ministries know of the laboratory, and look at it with respect. All the doors are open.

The California Public Health Foundation

Hughes: What about the public health foundation that you formed fairly recently? When was it formed?

Lennette: Actually it goes back to 1964. I was not one of the original people who formed the foundation. It was formed by Dr. Merrill, who was the director of health at that time or maybe deputy director, Bob Webster, who was the business manager, Bob Dyar, who was in the Division of Research, and a couple of people in Health Education, and so on. A small group, five or six, got together and formed this foundation with the idea of setting it up much as was done in New York State, where the foundation was set up to obviate all of the red tape associated with governmental operations. The foundation, as it was set up there, was really part of the New York State Health Department. It was autonomous, but it functioned through the department. It used a lot of their services, like personnel, purchasing, and so on, but, on the other hand, it was free to go out and do these things on its own, so that they could cut a tremendous amount of red tape.

Well, we just never got it off the ground here. So for many years, it was sort of fallow. It collected fees from the World Health Organization, which would send a visitor over here for a week or so, and then it would pay the institution five dollars a day for taking care of the visitor. That money went into the coffers of the California Public Health Foundation. Nickels and dimes business. Nothing very major.

Then when Mr. Reagan's administration came in, things got terribly tied up. Reagan and his crew from Sacramento wanted to run every little detail within the government, and he reached down into these departments as far as he could. I say "he--" I'm talking about his staff. They bypassed the channels. And they caused no end of havoc, no end of disruption. You just couldn't operate. In fairness to the Reagan group, I must say that the Brown group was no better. They merely compounded what Reagan had started, so that life today is almost impossible.

Hughes: Do you speak of both Browns?

Lennette: No, the older Brown [Edmund "Pat"], unlike his son [Jerry], was a statesman. I think the younger Brown is just a politician. He's looking to the next election. His father was looking forward to what's good for the state and country fifty years from now. Jerry Brown compounded what had been done previously.

Lennette: We felt we ought to take a good look and see if we could reinitiate, motivate this foundation, and get it off the ground. We made some inquiries about how to go about it. What we had to do was first look at the corporate charter, and then we changed it to fit our current aims.

We also had several people come into the department from New York State. Beverly Meyers, who was the director of public health during the Brown administration, had been in charge of welfare and Medicaid in New York State. She came out here with one of her right hand assistants and the assistant's husband, who was a physician and also a public healthier. They thought, when the foundation matter was broached to them, that this would be a good time to set the foundation wheels in motion.

Beverly Meyers had some years back been a laboratory technologist, so she knew something about the laboratory, knew what we were trying to accomplish, and she was very much for it. She was very favorable and very helpful. So was Don Lyman, who came in as chief of the Preventive Medical Services Division.

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We drew up some plans, a membership list for an advisory board, and so on. Then we had a meeting with Dr. Lyman, who was working with Bev Meyers. At that meeting we were told, "No, that's not the way to go. Our board has to be people within the government--just like the New York foundation. So this board will be set up with one public member. Dr. Lennette will be the public member. Then we'll have the director of finance and the director of general services, the director of public health, the director of whatever."

I said, "For heaven's sake, these are the people who give us the problems! Now you want to put them on the board? They're the ones that we want to get rid of! We don't want these people. We don't want to deal with them."

"Well, that's the way to go." So we turned over the charter and the corporation to this new group which was going to run this foundation, and they were going to set it up to reflect their ideas and wishes. It didn't take them very long to see that they were running up against conflict of interest laws, that you just can't use this kind of person. So they gave the foundation back to me and to Bill Clark to administer. Clark, however, had other fish to fry, so I ended up sort of the administrator, because being retired, ostensibly I had nothing else to do except twenty-four hours a day on the foundation. So I got Phil Brodzinsky, my former executive officer, who had retired, to help me. We began to look for grants and other sources of money and to follow things through. That's how we started, nickels and dimes.

Lennette: But people are strange animals. Very strange animals. For example, our great brains in Sacramento decided that all state units have to put a freeze on everything, on personnel, on travel, equipment, etc. "You see where we are; we've got to save money. Our budget is bleeding badly. We've got to save money," they say. So what do they do? They not only freeze hiring of state personnel and interdict travel by state personnel using state money, they freeze federal money, too. Now this is money that has been given to research people to do a specific job or piece of research. It's a contract. But they negate that contract by saying you can't hire any people and you can't travel.

The basic stupidity is well illustrated by the fact that one time we had a whole group of people here, venereal disease control officers, federal employees who were assigned to California, and whose salaries came out of federal monies given to Sacramento, but they were not permitted to leave the state to travel to Atlanta for a meeting of venereal disease controllers. Remember, these were federal employees paid out of federal monies, except it was funneled through the state. Of course this stupid act was resolved in a hurry. But we have the same or similar things occurring repeatedly. And each new administration begins anew with the same ridiculous behavior, unable to learn from the acts of their predecessors.

Anyway, we have the affected people, the principal investigators, complaining bitterly that Governor Brown (and Reagan before him) won't permit us to travel. Say they, "We have federal money. It's in the grant. It's been approved by the department of finance. It's been approved by everybody, personnel, and whoever else has to work on these. The money is available for travel to relevant meetings. Now the governor's office says nobody can travel out of state."

What happens actually, you see, the money isn't used. At the end of the year it lapses. The feds can't use it because it goes back into the general fund. The same with the state. Both are losers. The feds get mad about it, of course. "We give you our money and then you lose it for us." So the researchers are in a "no win" situation. Well, how can we get around that?

The answer is very simple. Go out and apply for your grants, apply for your contracts, but put them through the foundation which will control your money and will disperse the funds. If you want to go to Atlanta, or if you want to go to New York City or New Orleans for American Society of Microbiology meetings, and you're giving a paper, go. We'll just write you the check and pay your expenses. It comes out of your grant. The

Lennette: money's allocated, line-itemized. It's legal. If you want to hire two technicians and you need them next week for something special, go get them. You don't have to wait thirteen months. You know, to get somebody hired by that time--if the grants are for two years--means the first year's gone by before you get your staff, so you can't do anything much the second year.

The people who complained most bitterly about all of the restrictions, about all the hog-tying that was done by Sacramento, were the most resistant to coming into the foundation, to the point where I said, "Don't tell me all your troubles, give me all your grief. I'm not interested. There's a solution to your problem, but you're not willing to follow it." I presume they were afraid of rocking the boat.

Hughes: What a situation!

Lennette: Well, you lose your scientific reputation, too. You've got a grant that's awarded for three years, and then you can't turn out the work because you've got a freeze on employment, and you've got a freeze on ordering materials or equipment. You're dead. You can't fulfill your contract. So the next time, "Well, why should we give it to the people in Berkeley? They don't do anything. They just sit there on this contract." That's happened in other units of the department, too, not just the virus department.

Hughes: Do you have any more comments about funding?

Lennette: No, except to say it's very difficult now. Very, very difficult.

Hughes: On both levels, I would think.

Lennette: Oh, yes. Money has been cut back at all levels. And basic research is really suffering, which is too bad. And rather naively, government has assumed that industry, which has a big stake in the industrial research, would pick up the tab to support a lot of the research. They're not interested in that kind of research. They're interested in developmental things.

Hughes: Yes. You mean they're not interested in basic research.

Lennette: No. Well, with rare exceptions, like Bell Telephone Laboratories, which I think has a wonderful record of basic research. They come up with all these new inventions--like the chips. Transistors came out of the Bell Laboratories. Chips followed on that. But industry can't take over the whole workload. So you see, our political friends in the early thirties and forties killed off the golden goose that was laying the eggs, and now they haven't got any choice to give money anywhere. They can't get it from the

Lennette: goose. The goose is dead. And they have been profligate in spending their own money over all these three or four decades, five decades, now, since the thirties. There's little money left now. It's all sopped up by social programs.

As a matter of fact, I was at a meeting a few months ago at Peralta and Merritt and Children's Hospital, which are forming sort of a consortium, so that they have management uniformity, and they can run the administrative show conjointly to cut down on costs of managing the hospitals. One of the speakers at that meeting in 1982 was Paul Ward. Paul Ward goes back I don't know how many administrations, but he and his associates were responsible for writing the MediCal Act originally. He was the lead spirit.

He said, looking at it today he wouldn't recognize what the MediCal Act was as originally written, there's so much added into it and changed around. Furthermore, what the politicians, the legislature, have done about MediCal recently to resolve all these deficits sounds pretty good, he said, but the people don't realize that in about four or five years, when the full impact hits the public, that's when the roof will fall in. He said the people have not yet had an inkling of what's in store. They're beginning to get some now.

#### The Training Program in Diagnostic Virology (continued)

Hughes: I understand that the training program in public health microbiology was part of the original mission of the Virus Lab. Is that not true?

Lennette: The training programs go back quite a ways. They antedate my coming here in that, by California regulations, any individual who earns a bachelor's degree in microbiology then has to serve a six month apprenticeship in public health microbiology if he wishes to work in public health, either in the state health department or in an approved local public health lab.

Hughes: That's true today as well?

Lennette: Still true. So these people all came into one section or another. That was the training program. When I came here, I started the same thing for people in virology, but not necessarily at that level. These people at that time received a few weeks of virology added onto what that six months had been before. But I began to take in people from other countries. We had quite an international training program here. These are people at the doctoral level usually. Some at the bachelor's level. But we had a whole school

Lennette: of them. You'll see some of their portrait pictures in the virus lab library. That's only half of the people we've had. We never did get all our students photographed. And then, in addition, we had laboratory training programs for anybody in a state laboratory, in a public health laboratory, who wanted to come up and spend a week or two days or three days. That still continues.

Hughes: Was there a set course?

Lennette: There was also a set, formal course. Originally we gave a five-week course in virology, and we would take in, oh, maybe fifteen students. That's all the space we had. Then gradually we enlarged it, and we now have regular training labs which were built on the first floor in the new wing. We put in two training laboratories there, one for microbiology, and one for virology. We use them all the time. And that's what they're reserved for, because we still put on courses, in immunofluorescence for viruses, immunofluorescence for bacteria, or other new tests in microbiology, virology, or parasitology. Those labs are really used.

Currently we're supplementing that program with what we call Telecon. All the public health laboratories are apprised that on such and such a date we plan to talk about, let's say, the diagnosis of rabies using immunofluorescence techniques, and a small series of outlines is prepared, and, in some cases, even slides. They're sent to these local departments that have signed up, and then all of the discussion comes over the Telecon from Berkeley. The two people responsible will be sitting here in Berkeley, the tape will start, and the people at the receiving end have a chance to listen to the tape and compare it with their outline. If they have questions, then at the end of the hour the questions can be telephoned here to Berkeley. It's just like a conference call with ten or fifteen lines open, and it works very, very well. So that's been the latest addition to our teaching and updating program.

But we have still retained our formal courses. We feel that our mission now is training and research and development, and to support epidemiology.

Hughes: Would you say that the great bulk of the public health virologists in this state have received training here?

Lennette: Yes. Very likely.

Hughes: They would have to go out of state to get it elsewhere, would they not?

- Lennette: The Center for Disease Control gives courses, too. You have to remember, some of these people come on their own time. They can't afford to spend plane fare and living expenses in Atlanta for a week to take the course, aside from what the course costs them. They can come up here, and in two or three days we can give them what they need. Once a year we have a conference at Asilomar [California]. It's been changing location in recent years, but it used to be in Asilomar. All the public health lab directors meet. It's called the Association of California Public Health Lab Directors. We also have, on the last day or day and a half, people from academia--San Jose State, Sacramento, and elsewhere--who teach clinical microbiology. We tell them what the problems are, as we see them, and what the teaching deficits are. They take note, and then they implement these things. In return, they tell us what's wrong, what problems exist. It is an excellent partnership, a good return.
- Hughes: You might ask them to emphasize certain methods that are not widely known?
- Lennette: Sure. We have workshops in the preceding three days of the meeting. These are usually four and a half day meetings. Each laboratory will have one--Air and Industrial Hygiene, Water and Sanitation, Virus, Bacteriology, Food and Drug. People can sit there and ask questions. We'll answer them. Or if something is hot off the griddle, we'll give them a brief seminar on it. The people here are well trained. The only thing is, you have to fight all the time to get money from the state to do these things. It's so shortsighted of Sacramento.
- Hughes: State money supports that training program?
- Lennette: Yes. Well, people pay their way. But we have people up in Sacramento who want to do away with all this. They say, why do we need all this fancy training and bachelor's degrees in microbiology? Why not have upward mobility? Somebody can come in and wash glassware around the lab, and by osmosis they acquire all this knowledge and, given enough time, I suppose they could be the director of the laboratory. [laughter] This is the kind of mentality that you have up there.
- Hughes: What about people coming from abroad?
- Lennette: Oh, we have lots of them.
- Hughes: Do they have to fulfill any qualifications in order to be admitted?
- Lennette: No. We take them in, usually on the recommendations of the ministry of health of their country, or we know who the people are. Or the World Health Organization wants to send them to our labs for two months or three months. We take them in so far as we can.

- Hughes: Are the training programs general enough so that somebody coming in from, say, one of the African countries could benefit?
- Lennette: We tailor them to fit.
- Hughes: But you can't do that for the individual, can you?
- Lennette: Sure. If he comes in and wants to spend two months studying respiratory disease, we'll give him all respiratory disease exposure. Everything that goes with it. If he wants exposure to immunofluorescence techniques, for example, we'll give him that. That's a short one. And we'll show him the differences in reactions between the different viruses.
- Hughes: What if he is interested in learning the diagnostic procedures for..?
- Lennette: All right, then he spends three to six months and he goes right through the laboratory, all sections. I used to say this: "The minute you walk through that door in the laboratory, you're shorn of all your degrees. You have nothing. You walk in there, you're just one of the technical staff." In other words, I just didn't want them sitting around and telling the girls what they want to do, because many of them want to come in here as observers. They don't want to get their hands dirty. They just want to see what is going on. Sometimes you get this sense that the people at the bench are meaningless. Well, just because you're an M.D. or a D.V.M. or a Ph.D. doesn't cut any ice as far as I'm concerned. You're here to learn, and you go out there and you learn. You sit at the bench with my people, and if they tell you something, you listen. That's what you're here for.
- Hughes: Did people in general comply?
- Lennette: Yes, ma'am. Or they'd hear from me otherwise. If any of them were problems, and the kids told me about it, I used to call them in and tell them about it, straighten them out.
- Hughes: So I gather the methodology is general enough that they could then go back to their own countries and apply it to diseases which may not be very common in this country?
- Lennette: That's right. The only hang up is money. They can be very well trained here, but when they go back, they can't get the equipment; they can't get the reagents. You see, in some cases it's almost a waste of time to train these people, because you know full well when they go back to their country, the ministry of health will never give them what they need. Not because of ill will. They just don't have that kind of money, and there are more pressing social programs to which they have to give priority.

Hughes: Were you ever in a position to speak to the ministries of health?

Lennette: Yes, when I made that long six-week trip for the World Health Organization, I talked to the people in Ghana, Nigeria, and in the Cameroon.

Hughes: Did things change?

Lennette: Yes, I saw the other side of the picture, which I would never get sitting here in this office in Berkeley. I talked to these people, and they told me what their problems were. And when I was in Ghana, we went inland to a couple of clinics. Also in Nigeria we went to a rural clinic. It's a different world.

Hughes: You mean in the sense of the equipment available?

Lennette: What you can do, yes. I visited one clinic in Ghana, which had one microscope, an old single-barreled brass microscope, but it worked. And they had a nurse-technician looking at stool specimens, looking for parasites. She was alone there and doing a marvelous job. She was identifying patients who had these various parasitic infections, but the money to treat them is lacking. There is a surfeit of problems.

We get these foreigners in the American schools of public health, and we tell them all about sewerage systems and wells and how you do this and that. It has little or no relationship to what these people are confronted with at all. I think the way to teach these things is for the instructor to go to that country and see how they live and what their problems are. Then you can begin to understand what they're up against. But you can't say you've got to go out and dig so many miles of canal and line it with concrete and so on. You've got to find alternative methods.

Hughes: Are the training programs at other public health labs in other states similar to what you do here?

Lennette: I'm not too familiar with the one in New York, but I think it and the one in Iowa are pretty good, and there's one in Madison. I don't know how good that is. The two that you hear about are the ones in Iowa and New York. But Iowa has very little virology. It's mostly bacteriology and parasitology. What they do give is very, very good.

Hughes: Somebody from abroad interested in virology would probably be interested in this laboratory?

Lennette: Almost invariably. They come because of the reputation of the lab. And they go to CDC because that's the federal government laboratory, and it also is well known all over the world.

Hughes: How does the program at CDC compare to this lab's training program?

Lennette: I don't think it's as good because they give a lot of courses which are didactic, and they give some lab courses. I think one of the difficulties is that the training courses are given by people who come out of the training division, or, like myself, they're too far away from the laboratory to know what the problems really are.

What you need, and what I've always insisted on in our training course, is have it given by the kids who are doing the work. [pounds on the table] Forget the M.D.s and the Ph.D.s. Get the kids who are doing the work. They know what goes sour at the bench. They know what goes wrong with their reagents. They know what kind of stuff company X is producing, which is lousy. And they know that company Y produces a better reagent. They can tell you all these things. How would I know sitting here? And CDC, you see, if you're going to fault them on anything, it's the fact that they use people out of the training division, not the real hands-on people.

At one time they were giving a course on immunofluorescence, then a new technique. Well, Dr. Lyle Lyerla, a competent and very conscientious chap who was supposed to give it, came here to spend a few weeks with us to learn the basis for the test. A very good man, but he didn't have much of a chance down there to learn about it. Since, he's been doing a good job teaching this and other methodology.

Hughes: Would it be fair to characterize your program as an apprenticeship program?

Lennette: Exactly. That's how you learn.

#### Changing Emphases in Microbiological Education

Lennette: This is my complaint today about graduate education in this country in the biomedical sciences. There's no department that I know of --take a small department, let us say, microbiology--that can take in fifteen or twenty or thirty graduate students with a faculty of six or seven. In those old days, it used to be almost one on one. The professor, your preceptor, probably had two graduate students. Now he's got eight, ten, twelve. It's a mill.

So when these people get through--at least this is my interpretation--they don't know anything. So they have to take another two or three years at a paltry salary, a starvation wage, as a postdoc. In those days you didn't need a postdoc. You got all that as part

Lennette: of your doctoral training. By God, you got out there in the laboratory, and the preceptor was out there every day, either once a day or twice a day, looking over your shoulder to see what you were doing. If you had a problem, you always had access to him. Today you've got to wait days for an appointment to see your professor. There is virtually no true microbiology, as it has been defined in the past, being taught today.

Hughes: Anywhere?

Lennette: Anywhere. It's all biochemistry and genetics. You look at a roster of people who have Ph.D.s in microbiology from outstanding institutions, all of their courses have been in chemistry, physics, and genetics. Very little microbiology. Microbiology is the study of the microbe, what the microbe does in nature. What's it do to the soil? What's it do to the human being? What's it do to the animal? What's it do to the plant? What's it do to the environment? That's microbiology. But these people use an organism as a model for a system that they're studying. Sure, you're studying an organism and mutating it and studying its genes. That's not microbiology.

Hughes: What sort of microbiology is the medical student exposed to?

Lennette: The medical students are shortchanged, too, because they're given all this molecular biology, which is really not part of the trade. If you object to that, they say, "What do you want us to do, become a trade school?" And my reply is, "What's wrong with that? These people want to be doctors." If you're going to build a medical man, you've got to teach him something about disease. And he isn't going to know anything about disease unless you tell him something about pathogens. What does the organism do? How does it get into the body? When it gets in there, what does it do to the defense mechanisms? What kind of lesions does it produce? That's clinical microbiology. That's disappeared. Very little of it taught today. But that's not unique. That's happened in physiology.

We used to have departments called physiological chemistry. All of a sudden they became biochemistry. You ask these biochemistry graduates today, most of them don't even know what the normal blood sugar level is, or how much sodium chloride you have in the spinal fluid. That was all physiological chemistry.

Hughes: Do you think the current faith in antibiotics has something to do with this? That the M.D. thinks, "If I run into a problem with infection, I'll give my patient an antibiotic, and I don't really have to know much about that microbe."

Lennette: That's the wrong approach. He does have to know something about the microbe. You'd be surprised how little these physicians really know about infectious disease, how it should be handled. That's why we have so many of these hospital infections. Antibiotic-resistant organisms.

Relations with the University of California, Berkeley

[Interview 8: February 24, 1983]##

Hughes: I would like to start by talking about the relationship of the Virus Lab and the University of California, which of course is right across the street. I know you were a lecturer in the department of bacteriology between 1947 and 1958. Can you tell me how that was arranged, and what your impression of those years was?

Lennette: Yes. In those years virology was still a relatively young and developing field. It wasn't being taught in very many institutions. So when I came here, part of the agreement on my coming to the Department of Public Health was that the university would pay part of my salary on the basis that I would teach part-time in the School of Public Health. I participated in several courses. I was already here and on the campus when the people in the department of bacteriology expressed interest in getting virology taught. There was nobody on the faculty versed in virology, and I was invited to give the course, which I did for some years.

And then finally along came, as I sometimes put it, the bête noire of medical microbiology, which is molecular biology. The department of bacteriology got so enamored and wrapped up in molecular biology that everything else was pushed aside. So there was no spot for me in the department. Plus others, of course. The teaching of medical microbiology in effect came into the School of Public Health. So I had some participation in that, both here in Berkeley and occasional lectures in Los Angeles at UCLA.

Our participation in the activities of the School of Public Health went somewhat further, because originally the school was housed in a barracks type building up on the campus. T-3 was the number of the building. Charles Edward Smith was brought over from Stanford. He had a laboratory over at the old Stanford Medical School campus on Webster Street in San Francisco. So he came over to Berkeley as the dean of the school. And later, when the university obtained federal funding, that building that you see now across the street was erected.

Lennette: It, like this building, was inadequate to begin with, because both the School of Public Health and the Department of Public Health laboratories were built on monies which had been allocated some years back, before World War II, and had never been augmented. In effect there was no taking into account the ravages of inflation, so we got less building for the same amount of money.

We tried to get around that by using some of the laboratory space in this present building for the teaching of graduate students and postdoctoral fellows in microbiology. There weren't that many of them. There were only several at any one time. They would do their formal coursework at the university across the street and their laboratory work here. This was worked out between Dr. William McDowell Hammon, who was one of K. F. Meyer's disciples, and myself. Then, when he left, that program sort of disintegrated. He went to the University of Pittsburgh several years after we began the program. There didn't seem to be too much interest on the part of the people in the School of Public Health in maintaining this relationship, so that all the reasons for locating the Department of Public Health where it is at present disappeared. Proximity to the university. The only thing which persisted was the use of the University of California School of Public Health Library, plus the rest of the library system. That was the extent of our participation. And some teaching.

As a matter of fact, later on the teaching relationship was revived again. We took in some of their students. When we put in the big so-called Infectious Disease Wing in the back some years ago, we took in additional students who were working for their doctoral degree. I think Dr. Richard Emmons, my successor, believes this is well worthwhile. I think he'll pursue that, too.

#### The Reputation and Accomplishments of the Virus Laboratory

Hughes: I believe that the Virus Lab is unique in being judged to be on a par with the top academic departments of virology in this country. Can you say how that came about?

Lennette: That came about because---it sounds immodest---of my resolve that the department would have a good research program which would encompass both the laboratory and the field. My interests lay not in what later came to be molecular biology, but in epidemiology and immunology and virology. So at the very first when we started out, I tried to get together the best staff I could, and hand picked them, of course all this within the restrictions of the Civil Service. But I was very careful in choosing additional staff, and I think that on the whole it worked out well.

Lennette: It was rather unusual for a department such as this to publish as many papers as we did in the fields I have previously mentioned. Some of them were really, in a way, milestones. For example, we showed in this laboratory that mumps virus can produce polioliike symptoms, even paralysis, which is transitory but at least here's a virus which was never expected to do this.\* Now it had to be taken into account and ruled out in a differential diagnosis.

We did a great deal of work on Q fever beginning in 1949. And virtually everything that is known on Q fever and was done in this country was done between two large groups: Dr. Robert Huebner and his associates in Los Angeles, and we had our own group up here supported originally by funds from the National Institutes of Health and the Center for Disease Control. Between the two groups we rather thoroughly worked out the epidemiology of Q fever. Very little has been added to it since then. We showed that Q fever was not necessarily primarily a pulmonary disease, that people could acquire the disease without showing much in the pulmonary system, and that the disease not infrequently ended up with a hepatitis. This is now acknowledged and accepted.

So there were some pioneering efforts. We discovered a number of new viruses. For example, Turlock virus came out of mosquitoes captured in the Turlock area. It was identified in this laboratory as a new arthropod-borne virus.\*\*

And coxsackie A21 was identified as a virus associated with respiratory infections. At that time we called it the Coe virus after the individual from whom it was isolated.\*\*\* And another enterovirus, which caused epidemics of hemorrhagic conjunctivitis, was identified in this laboratory.

##[telephone interruption]

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\*Edwin H. Lennette, Gerald E. Caplan, and Robert L. Magoffin. "Mumps virus infection simulating paralytic poliomyelitis. A report of 11 cases." Pediatrics 25 (1960):788-797.

\*\*Edwin H. Lennette, Margaret I. Ota, Frances Y. Fujimoto, Anna Weiner, and Edmond C. Loomis. "Turlock virus: a presumably new arthropod-borne virus. Isolation and identification." Am. J. Trop. Med. Hyg. 6 (1957):1024-1035.

\*\*\*Edwin H. Lennette, Virginia L. Fox, Nathalie J. Schmidt, and James O. Culver. "The Coe virus. An apparently new virus recovered from patients with mild respiratory disease." Am. J. Hyg. 68 (1958):272-287. Nathalie J. Schmidt, Virginia L. Fox, and Edwin H. Lennette. "Immunologic identification of coxsackie A21 virus with Coe virus." Proc. Soc. Exp. Biol. Med. 107 (1961):63-65.

Hughes: In your dealings with groups and individuals outside of the lab itself, was there ever any feeling that because you were mainly doing diagnostic work rather than "pure" research, that this was somehow not as respected as what was going on in an academic lab?

Lennette: Yes. There was an air of snobbishness surrounding so-called basic research, which was considered to be an intellectual pursuit. Applied research was considered prosaic, didn't call for much imagination, wasn't challenging, and was work for hacks. All this was without regard to the fact that much of academia was comprised of second-raters!

We worked with a number of groups. We were very interested in doing clinical and epidemiological studies. So whenever a health officer had something interesting that might be looked into, we were always available. Same with clinicians.

For example, when Dr. Richard Leonards over at Children's Hospital in San Francisco was a resident he had a number of cases of encephalitis in adults, older people. These were people who had a history of recurrent herpes. We did the laboratory work and found out that these people did have herpetic infections, and that encephalitis could follow a recurrent episode of herpes. This was in considerable variance with the current dogma, which held that the first herpetic infections were usually mouth infections or skin infections. The virus then became latent and subsequently nothing would happen, except that there would be a recurrence in that same skin area. On the other hand, the primary infection might start out as an encephalitis. But recurrent herpes never ended up with encephalitis. Only the primary ones. Well, Leonards in effect had the data, and we had the laboratory facilities, and jointly we were able to show that this was not so. And that was quite a paper to get published. To overcome all the prejudices. This was not at all orthodox.

Hughes: Did you have trouble getting it published?

Lennette: Initially we had, yes, but people then realized that maybe what we said was so. We had pretty good data, pretty good evidence, based on a series of about five or six or seven patients, all elderly. That's the sort of studies we did over the years.

The legislature, on the other hand, had taken the attitude-- which I think in large part still prevails--that the health department, like any other state agency, should concern itself primarily or solely with practical, pragmatic, applied matters and leave the research, especially basic research, to the university.

More on Wendell Stanley

- Lennette: Our big defender was Wendell Stanley. He pointed out that there was room in the field for everybody, that the sort of things we were doing would never be done if they had to depend on the university because the faculty was not interested in this sort of thing. While we in the health department were doing a certain amount of basic research, we were doing it to get an answer to a practical problem. We weren't doing it merely as a matter of intellectual curiosity. His defense of our lab happened so frequently before legislative hearings that the legislature finally became convinced that there was a spot for us in this world.
- Hughes: Did Stanley have a particular tie with Sacramento?
- Lennette: No, but he was a Nobel laureate and he was the chairman of the department of biochemistry and virology, and a very respected scientist, well known. His word carried weight more than mine as a state officer would have.
- Hughes: Can you tell me about him as a personality?
- Lennette: Very outgoing personality. Very aggressive. He was a biochemist by training, and was on the staff of the Rockefeller Institute at Princeton, New Jersey, which is a veterinary and plant research institute. You have to go back to the thirties when he was working there. Nothing was known about the nature of viruses. Some people had shown that in infected plants (for example, tobacco mosaic virus) there appeared a very heavy protein. This didn't occur with animal viruses, so it was thought, well, maybe in plants this is a chemical procedure. You're dealing with an inanimate protein which replicates by using the cell machinery, as compared to a true virus which replicates in animals and doesn't produce heavy proteins.
- Hughes: That protein business was established before Stanley even got into the area?
- Lennette: It was just about that time that they were getting into it. It was people like Stanley and a few others who really opened up the field. There weren't too many actively working in the field of plant virology. Next to Stanley's work in the English-speaking countries was the Rothampsted Experimental Station in England, which was famous for its plant work. Still is.
- Hughes: That was due to the work of Frederick C. Bawden and Norman W. Pirie?

Lennette: Yes. As a matter of fact, Bawden and Pirie were on the same track as Stanley on the crystallization of tobacco mosaic virus. Stanley had gotten these protein crystals out of infected plants, and shown that they were infectious. His crystals would produce lesions in the tobacco plant, on the leaves. He also showed that you could transmit the infection through plants repeatedly, so it seemed this infectious material was replicating. He characterized the viral material pretty well, and he even got some data on the structure. Well, it was difficult for the scientific community to accept this. Although, as I said, nobody really knew what the nature of viruses was.

Hughes: Do you remember any discussion at the time?

Lennette: There was a great deal of discussion, because he came to New York City several times to give a seminar. We used to have seminars once a month on Friday afternoons at the Rockefeller Institute in New York--Sixty-eighth Street and York Avenue. Wendell came several times and presented his data, and most of the virology staff, which was essentially all medical in New York, was very critical and very biased against accepting this heterodoxy he was proposing. So at these meetings he took quite a tongue-lashing from his contemporaries and from the older, respected scientists. Here you had the long, dead hand of tradition holding something back, a truly important contribution to knowledge.

#### Concepts of the Virus

Lennette: After I left the institute and came back here to Berkeley, when I was teaching the virology course, in my lectures I mentioned that I didn't think that the virus was incorporating into itself the proteins of the host cell. In my estimate, this was just pure contamination because of the inadequacy of techniques for separating out the contaminating material, separating the virus from all the other background material in the cell. And what was that based on? How could I justify that?

Well, Joseph Smadel, at that time at the Rockefeller Institute also, had done a lot of work on electrophoresis. Electrophoresis at that time was a very new technique. That was the new fancy, the new fad. Everything was being electrophoresed. Later on, when they had high speed centrifuges, no matter what you had, you had to centrifuge it to justify your existence. Then later on you had to put it under the electron microscope.

Lennette: Anyway, Smadel had shown that vaccinia virus had a characteristic electrophoretic movement, that there was a characteristic pattern to the movement of the virus on this electrical field. He showed you could do the same thing if you just took inert particles-- he used collodion particles--and coated them with a nucleoprotein recovered from vaccinia virus. These particles would migrate just like vaccinia virus, giving an identical behavior pattern. This suggested that there is something in the virus that gives it this characteristic, and that it's probably a host contaminant which is carried over and Stanley wasn't recognizing it. Well, time showed that Stanley was correct, his detractors wrong. It does happen. But it took quite a while to get the philosophy nailed down, because we didn't have all the molecular biology methods that were subsequently developed.

Hughes: The basic genetic mechanism was supposed to be centered in the proteins, because people thought that proteins were far more varied than were the nucleic acids. Here you were dealing with something that was obviously replicating. Hence it was more likely that it was a protein rather than a pure nucleic acid.

Lennette: One school of thought looked at these as self-replicating proteins, for example, plant people. These heavy proteins, they thought, were self-replicating, because, if you put a little bit into another plant, you would have more of this protein. So it was self-replicating. Actually it was being produced, like other viruses, by the genetic apparatus, which is DNA or RNA, as the case may be.

Hughes: This was a difficult idea to stomach, wasn't it? I mean, that proteins could replicate?

Lennette: With the kind of knowledge we had at that time, you had all sorts of theories. For example, one theory was that a virus is nothing else than a piece of a chromosome which has been dislodged and gets into the cell and then begins to replicate, and by replicating produces the damage. Well, they weren't too far afield actually, if you think of oncogenes today.

But you see, a lot of things get overlooked. Actually, the role of DNA in viral replication was shown by Oswald Avery, Colin MacLeod and Maclyn McCarty. The latter two were young physicians working under Avery. They were disciples of Oswald Avery and worked on the pneumococcus with him. [Frederick] Griffith in England some years back had shown that you can use dead pneumococci of one immunotype or serotype, and mix them with growing pneumococci of another serotype. You'll have in vitro replacement of the capsule, and you'll then have a live pneumococcus of whatever the original living type was. In other words, you had mutation going on. Avery and his two students showed that this transformation process was attributable to the DNA in the live organism. Nobody knew much about DNA. It was

Lennette: just another chemical. But the Avery trio showed that apparently the genetic material was responsible for transformation.

Well, that just lay fallow. Nobody paid much attention to it. So if you're going to talk about the Watson-Crick hypothesis and the working out of the structure of DNA and RNA, the genetic code, you have to go back to people like Avery and his group, who should have been brought in. But that's another story. It's like Rosalind Franklin, who contributed so much to the unraveling of the genetic code, being left out by Watson and Crick. A lot of people merit credit. Nobody makes a big discovery all by himself. There are others involved; you build on the foundation which has been laid by others before you. And I don't mean just by a colleague or a contemporary. Some of these things rest on a foundation that goes back fifty, sixty, a hundred years.

Just the other day I was looking at the New England Journal of Medicine. There is a two-part article which appeared, discussing the prostaglandins and the hormones and the neurotransmitters. Right in the very first paragraph they mentioned that the identification of a neurotransmitter as having hormonal properties is not new, because this was described some years back by Ernst and Berta Scharrer. They were refugees who came to this country from a German university. They were in the department of anatomy at the University of Chicago studying amphibians and frogs, and showed that in these animals there occurred within the nervous system what they called "neurosecretory granules."

They heard that I was working on poliomyelitis and using quite a number of monkeys, and wanted to know if they could look at the material and if I would stain some up for them during the course of my work. So as I did these postmortem examinations on the spinal cord and processed the tissues for sectioning and staining, I ran through some of their special stains, and sure enough, within the anterior horn cell neurons on the spinal cord you could see these beautiful red granules which, according to them, had a neurosecretory function. Well, they put my name on this paper along with them,\* and we had a hard time getting that published. Now you see, it's accepted. Like many others, they were too far ahead of their time, pioneering a field that wasn't ripe for exploration.

Hughes: That work just lay fallow?

Lennette: Yes. Now we accept that this substance is a prostaglandin. It can have both a hormonal function and can act as a neurotransmitter. They are not antagonistic functions. We did the same thing with interferon. I think I mentioned it earlier, didn't I? We went to a certain stage and that was as far as we could go.

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\*Edwin H. Lennette and Ernst Scharrer. "Neurosecretion. IX. Cytoplasmic inclusions in peripheral autonomic ganglion cells of the monkey." The Anatomical Record 94 (1946):85-92

- Hughes: Getting back for a moment to the concept of the virus in the mid to late thirties. If I remember it correctly, the first book that Rivers published, which I believe was 1927 or 1928...
- Lennette: Nineteen twenty-eight.
- Hughes: I believe that he encompasses several concepts of the virus, namely, that some viruses can be small microorganisms. Others may be enzymes or proteins, but with some mechanism of replication. Do you remember that phase in early virus research?
- Lennette: Actually, it wasn't a textbook. What he published was a series of lectures which he gave. I think they were called the Lane Lectures, which he gave at Stanford in 1927, I think it was.
- Hughes: There were several authors, I believe, in the book that I'm thinking of, mostly Rockefeller Institute authors.\* There was a paper in this book--in fact, I think it was the first paper--that was written by Rivers. I can still see in my mind's eye the table of the known viruses that he devised, and an attempt at classification. Most of them he thought were minute microorganisms, small enough to be filterable and invisible in the microscope. But then he didn't know what to do with the tobacco mosaic virus, so that was thrown into another category.
- Lennette: They appended labels such as "filterable" virus or "ultramicroscopic" virus, because the state of the art was such that we couldn't go beyond that. But eventually those terms were dropped, and we just referred to "viruses," because we realized that even these large particles behaved just as the small ones did, demanding growing cells, and they were strict parasites, and so on.

The big division in biology between prokaryotic cells and eukaryotic cells is that a prokaryotic cell has no cell membrane around the nucleus, plus certain other characteristics. But that's essentially the difference between it and a eukaryotic or true nuclear cell which divides by the chromosomes separating, and reduction division and all of that, which the prokaryotic don't. They are very primitive organisms which replicate by simple binary fission.

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\*Thomas M. Rivers, ed. Filterable Viruses. Baltimore: Williams and Wilkins, 1928.

Lennette: Lynn Margulis has written a book called Origin of Eukaryotic Cells, which I think is a classic, beautifully written. She just right from the very first throws out all the viruses. She says, we won't talk about them because nobody knows where they came from or how to classify them, which is quite true because we don't know what the ancestral cell was. We can kind of guess, piece together the information for eukaryotes and prokaryotes, but somewhere in the early beginning the viruses arose. I say this because one of the concepts of the virus was that this originally had been a free-living organism that became parasitic and as a result of its parasitism lost many of its functions and depended entirely on the cell. There's no way to prove that. But the eukaryotes arose by the fact that the original precursor or progenitor cell was probably invaded by bacteria which then just liked it and stayed. They then later on became mitochondria or chloroplasts, as the case may be, and now they persist and play a role in the function of the cell.

Hughes: Do virologists worry much these days about such questions, the origin of viruses?

Lennette: No, most of them don't. I think it's typical of graduate students, that when they get into a field, they think they're entering at the very beginning. If there's any past, it can't be more than four or five years, and any beyond that is just Neanderthal. Well, I assume that I had the same attitude, I don't know, when I came into virology in 1930-31. There wasn't very much known, really. It was a field that nobody with any sense would ever get into, because it was difficult. You had to work with animals. It took forever to get your experimental results. Hence, just stay out of it, and go into the genetics or into the physiology of bacteria. That's much more rewarding careerwise and on the academic ladder.

We weren't permitted to do this, going back into history only five to ten years, because we had a young professor, Paul Hudson-- he was about thirty-five or so when he came to the University of Chicago--who was most exacting. He had been a member of the staff of the Rockefeller Foundation, had been stationed in West Africa, as I believe I told you, and was one of the triumvirate that first isolated yellow fever virus and characterized it. And then he came to the States to teach at Chicago. He was very demanding, and he wanted you to know what all of the outstanding names were, not only in the history of virology, but also in contemporary virology. There weren't all that many, however. But you had to know who was doing what and why. And you were quizzed on that. He had a seminar with his graduate students-- he had about five or six--every Saturday morning. Then he would quiz you on the current literature so that you had to be on your toes. He was a hard taskmaster.

Lennette: You don't find that today. Part of our doctoral requirement in those days was the ability to read French and German, which has since disappeared, because all the translation is provided today as a routine. Much of the voluminous literature is summarized in computers, so not to worry about that. We had to find the original articles and translate them. Even [Jules] Bordet's original papers, written back in the early 1900s in immunology, you had to be familiar with. But that was part of the educational process.

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Today the professor has so many students to take care of that graduate students just become lost in the structure somehow. They don't get the attention that we used to get. And this is why, in my estimate, students are being shortchanged. When I was a graduate student, some of us went on to postgraduate study, but mostly for a year or so just to sharpen our skills and our knowledge. Spend a year in Rothampsted or a year or two at the Rockefeller Institute. Now a three to five year postdoctoral training program is part of getting your degree. Why is that true?

In my estimate it's true because the teachers in the graduate schools are at fault. They try to do too much with too many students. So as a result, the student doesn't get what he should be getting, the personal attention that students used to get from their preceptors. So they have to make it up elsewhere. So what do they do? They have to take another three to five years in some institution, and I'm not sure that they always get value received. Some of them end up as mere technicians with a doctoral degree. Very cynical, but nevertheless true. I'm on the side of the students, as you might gather.

#### Recombinant DNA

Hughes: Shall we move on to DNA?

Lennette: Paul Berg, a biochemist, was working on recombinant DNA techniques at Stanford. Now, this is all secondhand that I got through the grapevine. One of his students, or maybe several students of his, were at a meeting at Cold Spring Harbor, New York, a molecular biology meeting. One of them, a woman, happened to mention casually some of the experiments that the Berg group was contemplating. The listeners were horrified at these experiments, because they might create genetic monsters or Frankensteins, and be catastrophic. You'll create something which, if it got loose, would be very destructive to the environment or the world or whatever. The scenarios were pretty lurid.

Lennette: In great distress, apparently, she telephoned back to Dr. Berg. Well, anyway, they gave all of this another thought and decided they wouldn't do the experiments. They would hold a meeting of concerned persons at Asilomar, California, to which they invited a lot of the top molecular biology people. They called in attorneys, and university officials, and, not least, bioethicists. This was an international meeting.

And out of that meeting, after they had discussed all these aspects of molecular biology--recombinant DNA, really, which was a technique that Paul Berg had devised, and for which he received the Nobel award--they decided that they ought to have a moratorium until they had a better idea of where they were going. A letter to this effect was published in Science, advising the scientific community of what had transpired at Palo Alto, the so-called "Berg letter."

I saw the letter in Science and immediately wrote to Berg pointing out that I could understand his concerns and his motivation in calling the meeting and coming up with that document. But I felt that if he had had at that meeting some people who were infectious disease experts, well trained in medical and pathogenic microbiology, that what they had written would be quite different in tone and in outlook. Well, he never answered that letter. I know him. He probably got so many letters from people like myself he just threw up his hands and decided it wasn't feasible to answer them all.

Hughes: What year was this?

Lennette: Oh, this was back in 1975. The Asilomar letter, I may have it here. [interruption while Dr. Lennette looks for copy of letter]

Hughes: It's right here, 1975.

Lennette: As it turns out, and on several other occasions, other scientists besides myself have mentioned that while these people were experts in biochemistry and in genetics and biophysics, they didn't know anything about containment of pathogenic organisms. And in one of my epilogue papers that I prepared for Perspectives in Virology--these are generally held every two years in New York--I pointed out that there's a long record of handling pathogenic microorganisms, that you can handle these with care and that you don't have any problems. It's only when you disobey all of these precepts and things that we've learned just by experience that you get into difficulty. There's nothing ever been laid out as a one, two, three, how you do these things. You learn at the bench. The way I was taught, we had four or five graduate students and the preceptor was there in the laboratory with you. He saw how your techniques were being developed, and he made sure that you had good work habits and weren't sloppy and spilling everything all over the place.

Lennette: You don't get that today. A student comes in and he signs his name on the roster, you hand him a laboratory coat, point out the door to the laboratory, and say, "Go do it." And he has no really close supervision. Not that a professional biochemist or geneticist needs that kind of training. But if he's going to get into a world where disease prevails, he'd better get some of that because of the sort of things that we deal with.

For example, in this laboratory, we don't know what comes in the front door and what we're dealing with, whether it's going to be potentially lethal or not. So we handle it with a great deal of respect. We don't get sloppy.

So anyway, these molecular biologists have learned how to do some of these techniques. I think they still have a ways to go. And none of the things that were prophesied, these horrible scenarios, have developed. That's not to say they can't. If somebody wants to incorporate some kind of a gene which is detrimental or noxious into an organism, I suppose he could do it with great ease. Just as a terrorist can make an atom bomb. I don't know of any way to preclude that happening. But all the horrible things that were going to happen to the environment and all of the monsters that were going to evolve, all the Frankensteins, it just hasn't come to pass. As a matter of fact, one of the big problems today is they can get these genes into a cell, but they can't get the genes to express themselves. So it's the other way around.

There was another meeting at Asilomar. I don't know the year, but it was on biohazards, not specifically directed at recombinant DNA techniques, but across the field. And at that time I gave a paper down there on--a little out of my field!--bacteriology. I think it was on tuberculosis. How you handle these organisms. All I can remember about that conference was we spent two and a half days telling the audience what the hazards were, and they all left. The biochemists weren't at all impressed. And I don't know whether that meeting antedates the Berg Asilomar meeting or followed it. I think it followed it. Jim Watson was at that meeting. He was a little concerned about the biohazards involved.

Hughes: At some point the recombinant DNA people began to pay attention to what you people in pathogenic microbiology had known for years. Is that not true?

Lennette: Well... they began to learn, because they were afraid of what might happen if these organisms got loose. They had to learn how to contain them.

Hughes: How do you suppose they learned?

- Lennette: By going to other laboratories and working with people. I'm not so sure that their techniques are all that good. When I expressed myself originally, I thought just like the communists: You can't work on this generation, so work on the kids. [laughter] You can't retrain these people, because they'll never be very good retrainees. Start with the young students. Teach them properly.
- Hughes: In this paper that you gave in Britain, you suggested establishing extramural safety review committees to "examine methods, techniques and operations with respect to safety."\* Did they pay attention to that?
- Lennette: That paper was read for me, because I had to chair another meeting in Geneva. I was in Geneva, and expected to get back to present that paper at Y college, but unfortunately I was made chairman of the Geneva meeting, so that destroyed my ten o'clock meeting. I don't know how that paper was accepted, but I would think not with any great enthusiasm.
- Hughes: Is there anything more to say about your contact with that particular recombinant problem?
- Lennette: No, except that I've been following all the recombinant DNA work with considerable interest. I'm not a practitioner of it, and I don't always understand the genetics and the biochemistry involved--it's a field in itself. But I've been following, for the interest that I have in pharmaceuticals, chemotherapeutic agents, and also the production of vaccines. I think those are the two big areas. So if we could produce hormones, for example, simply and efficiently and cheaply, that would be a great step forward. The other is to produce antivirals. And that's a whole field. Well, not antivirals, but really vaccines. The current vaccines, as you know, usually incorporate the whole organism, much of which is useless. It's extraneous material, serves no good purpose, and if we could just get around that by using only those components or those constituents which protect the individual, we would go a long way.

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\*"Recombinant DNA: A Public Health Viewpoint." Reprinted from, Recombinant DNA and Genetic Experimentation. Edited by Joan Morgan and W. J. Whelan, 261-276. Oxford: Pergamon Press, 1979.

Lennette: Now, synthetic vaccines are being looked at, and one of the leading people in this field is Richard Lerner at the Scripps Clinic in La Jolla. He's done a great deal of work on the subject. As a matter of fact, he has a lay article in one of the Scientific Americans. I haven't seen it, but I've heard of it, and apparently it's the way to go. Of course this isn't new, because Michael Selas of Israel mentioned this, oh, twelve years ago, I guess, at one of the Perspectives in Virology meetings. And I've mentioned this myself. One of the ways of doing influenza vaccine, to prevent all of these reactions that people complain about, is find out what really is protective. Is it the glycoprotein or it is the matrix protein? Probably glycoprotein. Get this constituent out and make a vaccine out of that.

Hughes: Is anybody trying to do it?

Lennette: They're working along those lines. Now, it may not be quite as simple as I put it, because you may get this purified thing which is responsible, but if you get it real pure, it may not act. You can't always win out.

Hughes: Do you think that the guidelines that were established for research with recombinant DNA infringed upon the scope of research?

Lennette: Yes, they did impinge as far as the concept of research is concerned, the intellectual freedom. The physical guidelines, I think, were good.

Hughes: You're talking about the degrees of containment?

Lennette: Containment. So those, I think, were good. I don't know how well they're followed. Probably not very closely. This is my judgment of how people behave. [laughs] But I think intellectually it did have a negative impact. I can't put my finger on it, but that's the way I feel about it. And I could side with the people who held this opinion. Being a scientist myself, I just don't like to have restrictions put on what I can do and what I cannot do. And sometimes we have to do things just out of pure curiosity.

One time I was trying to arouse interest in the development of a vaccine for mumps. Well, I never got around to developing it. So other people have been doing this sort of thing. And then at one meeting at NIH we were talking about the vaccines that were available.

##[telephone interruption]

Lennette: I was chairing the meeting, and we were discussing vaccines for children, respiratory syncytial vaccine, parainfluenza vaccines, measles, and so on. All of this to protect children so that they get through all the vicissitudes of childhood and develop into virile adults, I guess, with no problems of illness. At the other end of the corridor, the extreme end, was a conference on world population and how to contain it. Both sponsored by the same institute. I did a double take, because it didn't make sense. Here we're trying to preserve all these young people at one end of the scale, and at the other end they're trying to figure out how to stop all this. So I suppose you probably end up the way they are in China, limit all the families to one child.

#### Administrative Duties

Hughes: I know you stopped doing laboratory work at some point because the administrative burdens became just too heavy. Can you remember when you no longer were doing bench work on a steady basis?

Lennette: Oh, it must be about twenty years, which would make it about fifteen years or so before I retired [1978]. The staff became very large... The size of the staff was not my doing. I was not an empire builder. For a civil servant, I guess I didn't fit the pattern, because I tried to keep the operation small. It was my superiors who built the thing up, to the point where I just didn't have time to do both. And my career has changed. In the early days, when I first started out, I used to see patients occasionally, infectious disease service, and could empathize with them. And then as things got more involved in the laboratory, I spent more and more time in the lab, actually, and less and less on the clinical bit. Of course, that was just a matter of a few years. And then as the laboratory grew, first because of the poliomyelitis problem, and later on the cancer project, I was just overwhelmed. I couldn't handle it every day. Like some of my colleagues, I wrote out all of the research grants myself, so I spent a lot of my time keeping abreast of the literature, writing the grant applications, figuring out budgets. I had two very good staff people. Nathalie Schmidt then just took over charge of the laboratory for me by indirection, and Robert Magoffin was the executive officer and handled the clinical and epidemiological end when physicians called us. So we had a very good team of three people at the top of the operation.

Lennette: But to answer your question more directly, no, I just had to drop out. Now, that doesn't mean I didn't have interest, because I had to know what was going on. I used to go into the laboratory and talk to people about what they were doing and how they were doing it and give them suggestions or ideas.

Hughes: They would come to you?

Lennette: Oh, yes, they came to me occasionally. Once you're in the laboratory and you've got a program going, you're pretty busy. So I would try to catch the people in their office or when they weren't tied up in the lab. I tried never to bother anybody who was working in the laboratory. Even a technician who's doing anything at the bench. You don't do that, because it distracts them.

Hughes: So there was no real structure to how you kept in touch with what was going on in the lab?

Lennette: No. It was on a very informal basis. Now, on the other hand, I don't want to leave the impression that the laboratory was very loosely or even sloppily operated or run. The operation here always had a reputation for being a very tight show. I, with the help of my staff, picked all the technical staff. We didn't just take people willy-nilly off the Civil Service list. They had to justify their position. We wanted to be sure that they were compatible. What's the point of having a genius if he disrupts the whole laboratory? You can't afford that. So we had a very good staff. And the show was very tightly run. And that reputation preceded me all over the country.

People had to get here on time. Eight o'clock in the morning was the starting time, and I didn't accept any excuses. My attitude was, the State of California gave you a job from eight to five. I expect if you have to come from Reno, be here at eight. No excuses. "Well, my earlier bus gets me here at twenty minutes of eight." Then come at twenty minutes of eight. I was very hard on that. And the same way on coffee breaks. Because a lot of things get started in the Civil Service, and I guess in industry, too, that pretty soon people look upon as a right and not as a privilege. I had to disabuse them of that. I was pretty rough on it. Of course, I was in hot water all the time, with people getting up on their hind legs and saying that I was violating their civil rights or their whatever rights. I look at the world today as being made not to do anything worthwhile. It's made to suit the individual employee, never mind the greater glory of what you're trying to accomplish.

Professional Associations

Hughes: I find that there are about nine pages in your curriculum vitae on professional associations and memberships and consultancies. I thought that the way we would start, if it's all right with you, is to talk about the associations of which you were president, and then we can pick up any others that you think are significant. Just to refresh your memory, there were five associations of which you were president.

The Tissue Culture Association

Hughes: The first one is the Tissue Culture Association, which, I understand, is rather a small group. Do you remember when it was founded and what the impetus was?

Lennette: Yes, it was started right after the war. Tissue cultures were being used in virology, but they were rather primitive types. Virologists were interested in tissue cultures as a means of replacing animals, which were so costly. So the society was founded by people like Thomas Francis and Jerome Syverton and Joe Smadel from the Rockefeller Institute, myself, and several others. Then other people got involved in it. Originally it was just a very loose confederation of people. The secretary, whoever he was--I can't remember now--was charged with getting out a newsletter periodically, and it came out with that purple ditto ink, where you use gelatin.

Over the years it became more formal. I dropped out, but others came in. They eventually made it the Tissue Culture Association and began to teach courses. The courses were given up in New York State in various little cities. Wherever there was a small college or university which had laboratory facilities, they would give the course. Primarily it was given at Cooperstown, New York. That course was given for some years. I was never really very active in the association, because my interests lay elsewhere--immunology, virology, and epidemiology.

Then one day I got several phone calls from people saying, "This association was started with the help of virologists, and we haven't had any virologists on our council or in our offices for years, and could we put your name up for the council?" I saw no great objection, although I didn't know how much time I could give it. By this time I had a certain reputation for administration, deservedly or not. As I found out later on, they had problems running that society, the usual headaches, to

Lennette: get people to do things. I got elected to the board of trustees, much to my surprise.\* I didn't think I would. Who ever heard of me in the cell biology group? Apparently my name had spilled over from other disciplines.

Hughes: Were the cell biologists the main component of the Tissue Culture Association?

Lennette: Yes. I didn't think anybody knew me. But apparently, as some active people do, their name spills over into other disciplines. So I was elected. At my very first meeting of the council, which was in Washington, D.C., as I remember, I was provoked by the chairman of the program committee, who appeared before the council members and said he had to have more money and was inviting all these people from abroad to give these special symposia and colloquia, and why was the society so niggardly in providing him with the funds. Well, it isn't a very big society to begin with. And secondly, I just pointblank asked, "If we're so devoid of talent in the United States of America that we have to go abroad to Europe and elsewhere to get competent speakers, I think we ought to just close out this society, because there's no point in having it."

He said, "If that's your attitude and you don't give me what I need, I resign."

I said, "It's accepted." I'm a council member. You're supposed to bring this to a vote. I just took it upon myself. I said, "We accept it." Everybody was stunned, because this isn't the way the people had been behaving. They had never faced up to their problems. They just let them ride. So you have a continual perpetuation of administrative problems.

Well, after this chap cooled off a day or two, he came back and everything was forgiven. So he stayed on. But that's the sort of thing it was. Eventually they ran me for president, and I was elected president, a two year term. Tremendous number of problems that had to be resolved--fiscal problems, administrative problems, and how to run the society better and all the meetings. It's a small society so that the officers, especially the president, had to carry a pretty heavy load. Just like the big ones. Like the ASM [American Society for Microbiology], where we had thirty-some thousand members and a big staff in Washington. In the TCA, you did it all by yourself.

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\*Dr. Lennette was a member of the board of trustees from 1970 to 1974, vice-president 1973-1975, and president 1978-1980.

Hughes: Was there any paid staff?

Lennette: Well, we had volunteer staff. Later on we got a paid staff. Then I served those two years as president and then went off and retired, and apparently some more problems cropped up, and by this time they wanted me to run again. I said, "Why do you need an old retread? I've been president once. Who wants to vote for me a second time? Why don't you get some young person in their forties? Let them run the shop." Well, "We need your background."

Hughes: They were thinking of administrative background or your scientific experience?

Lennette: Both. And I said, "All right, fine." I didn't think I would be elected. But I was, the second time around. Well, I never got to hold office, because by that time I had been up at Lake Placid and I was supposed to come in in June, 1982, and I just resigned. I resigned immediately after the death of my wife in '81, because I didn't think I could carry that load. And then they asked me to reconsider and I did and I resigned a second time. Gerard McGarrity then became president. So that was my experience with the Tissue Culture Association.

Hughes: Are virologists still a great minority in that association?

Lennette: Yes, pretty much. There are some papers given on virology, but not very many. That has never been a very strong focus for virology. Most of virology has been in the American Society for Microbiology. And that's passing, too, as I'll tell you in a moment.

Hughes: One little aside about tissue culture--did you have any personal contact with the HeLa cell line, and did it really make an impact on cell biology and on virology?

Lennette: Yes, it did. It had a very broad application in many fields, not just virology, but in medicine, infectious disease, immunology, cell biology, biochemistry. Jerome Syverton was a virologist who popularized it. He was professor of microbiology at the University of Minnesota. He's worked on polio. The HeLa cell is an immortal cell, a continuous passage cell. It came from Helen Lane. The first two letters are her first name; the second two are her last name. That cell worked out very well, and we used it here in this laboratory. It was one of the first ones that we had. Then later on when Enders and Weller and Robbins showed you could use monkey kidney for so many things, that became the other standard line.

Hughes: Did it matter to a researcher which line he used?

Lennette: Originally we didn't know all these differences. These came out with time. The HeLa cell line is so easy to maintain, because you just pass it from tube to tube or flask to flask, whereas a monkey kidney is a primary cell line. You take the kidneys and you make up a lot of cells, and then that's it. You can't carry it very far, because it will die out. We used monkey kidney a great deal, as well as several other lines in the laboratory.

#### The W. Alton Jones Cell Science Center

Lennette: But the HeLa has an interesting background, because this was started by George Gey.

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You'll find out in a moment what I'm leading up to. While he was working on HeLa cells, a line which he and his wife Margaret had initiated and characterized, and doing other cell biology, he had a young student, Patricia Jones, who was very much interested in cell biology. She had done her undergraduate work, I think, in chemistry. Patricia's mother used to come down to Baltimore occasionally to see her daughter Pat, so Pat took her mother into the laboratory one day to see the kinds of things they were doing, and showed her cells under the microscope. Her mother's name was Nettie. Nettie was very much interested in the things she saw under the microscope, and then she met George and Margaret Gey. They're a wonderful couple. And one thing led to another.

Mr. Jones was a midwesterner who was working for an electrical utility in Oklahoma somewhere, as I recall. This utility eventually took over some oil holdings, and so they ran an electrical utility, and also were producing oil. And then because of some legal point, the utility eventually had to divest itself of one or the other to break it up, and they asked W. Alton Jones, Pat's father, what he would like to do. Do you want to stay with the original electrical company or do you want to go with this new company? Well, he'd go with the new company he thought, which he did. Eventually he became chairman of the board of Cities Service. A huge operation, as you know. Became very wealthy.

The Jones family later moved up to New York State. They had a summer place up in New York State, and the stories that I get on Alton Jones was that he would fly over upper New York State (if he was up in the New York office in New York City) and if he spotted a good piece of land, he would buy it. So on one occasion he had to be up in New York City for a meeting. I don't know whether he was going to to Lake Placid or not. They had

Lennette: several big homes up in Lake Placid. As the company aircraft was disabled for whatever reason, and he wanted to get to New York in a hurry, he called one of his friends, the chairman or president of American Airlines, who got him a seat on a flight which crashed up near New York. Jones was killed.

Well, to get back to what I started out to say. Mrs. Jones thought that putting up this W. Alton Jones Cell Science Center would be a good memorial to Alton, who was buried near the village of Lake Placid, as I recall. She had expressed interest in the Tissue Culture Association, and some of the people in the TCA, like Sergei Fedorov, Donald Merchant, Louis Coriell, and Vincent Monroe, eventually convinced her that it would be nice to have a tissue culture center up in Lake Placid. They wouldn't have to do all this moving around to teach tissue culture. And after due thought, I guess Mrs. Jones thought this would be a good idea, too, so she funded it.

Hughes: You mean it's primarily a teaching institution?

Lennette: No, that's how it got started because they wanted a home for the teaching which they were going to do, and research was essentially secondary. So Mrs. Jones gave them the money, five million dollars to put up a beautiful building. It is architecturally very aesthetic. But in this day of energy conservation, it's dreadfully expensive, because it has huge plate glass windows with wonderful vistas of the countryside, but the heat just roars out of there like mad, and of course, on the other hand, when you're trying to cool that building, you've got a lot to overcome.

But Mrs. Jones was, and is, a good patroness. She was very generous. So that's how this center was set up.

Now, more recently, through a number of things that have happened, Patricia--her married name is Edgerton; her husband's a plastic surgeon at the University of Virginia--Pat Edgerton and the Jones Foundation, which was supporting the center, came to loggerheads with the Tissue Culture Association. Mostly personalities involved. But other spinoffs were involved, too. It's a complicated story. The differences came to the point where support was going to be withdrawn by the foundation, and the Tissue Culture Association had no choice but to give in and deed back the property to the Jones Foundation, which is now using it for teaching and research, but mostly research.

I was up there for six months, as I told you, as the interim director until they could straighten out their affairs.\* They have a new director, Dr. Gordon Seto, coming in the first of July [1983], who is from the University of California

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\*Dr. Lennette was interim director in 1981 and 1982.

Lennette: at San Diego. He's a cell biologist. He's also bringing with him one of his colleagues to do all the administrative work, fiscal work. So two people to do the job I was doing. Of course, they won't get ulcers the way I did, either. So that's where it stands. And there's a lot of bitterness on the part of the association.

Hughes: So they're left without a home, virtually?

Lennette: Well, there are some legal involvements, too. Considerable money was given by the Tissue Culture Association in terms of endowment, and they're trying to get that back. I don't think that the Jones Foundation will try to keep that, and will give it back to the TCA. But it's an unpleasant situation which I think, with a little more flexibility on the part of the people involved, could have been resolved amicably.

#### The American Society for Microbiology

Hughes: You were president of the American Society of Microbiology in 1978.

Lennette: I was a member of that association for many years, and I never bothered too much about offices. I helped to found the American Board of Medical Microbiology and was one of the charter members of it. I brought it to its early infancy, along with a lot of other people. That's where my interests lay.

An organization like the American Society for Microbiology is open to all people. It doesn't take any special background or you don't have to have any great reputation to become a member. Just pay your dues and you're a member. That's what makes it so large. But with typical academic misperception, you would occasionally get nominating committees who would nominate some illustrious scientist to be president, not infrequently someone who had never been to a meeting, but who served as president and gave his presidential address and you never saw him again. The society can do without people of that kind. Sure, they give you some prestige, and it's an illustrious name, but they don't contribute anything to the operation of the society. What you need are people who are dedicated and who are workhorses and who really have an interest in doing it.

So when you get nominating committees which are willing to look at candidates from that standpoint, then you've got a different kind of a cat coming in as president. And that's what happened here. Phil Gerhardt called me from Michigan State University in

Lennette: Lansing, Michigan, and finally broached what was on his mind. He said that he wanted me to know that the nomination committee suggested he call me to see if I would be willing to run for president of the ASM.

I said, "You're out of your mind. Why should I run at my age? Nobody knows me anymore. You've got a whole two or three new young generations in here. Why don't you get somebody who's active? I'm retired."

Well, "Think about it for a while." So Gerhardt called me back about three weeks later, and he really worked me over and gave me a lot of reasons. I finally just caved in. I couldn't resist all the blandishments that were being offered as president of the ASM. I said, "All right. I'll do it." It was a very delightful year.

Hughes: Was it at all unusual to have a virologist as president?

Lennette: No, there had been several others. Bill Hammon was a virologist. Mostly they were bacteriologists.

Hughes: But was there any feeling of division between the microbiologists and virologists in the early days?

Lennette: No.

Hughes: You as a virologist were always welcomed on a par with microbiologists?

Lennette: Yes. As a matter of fact, we old-time virologists took the position that you couldn't do good virology unless you had a good background in bacteriology. And in my time, what you needed was a good background in bacteriology, immunology, and pathology. Today that's all different. It's all biochemistry and mathematics and genetics. But there were no antipathies. Well, we changed the flavor of the society.

I was one of that group of five or six presidents who, serving in succession, were able to radically restructure the society.\* Beginning with Helen Whitely of Seattle, then Harlan Halvorson of Brandeis, Fred Rasmussen of UCLA, myself, Willis Wood of Michigan State, and Albert Balows of the Center for Disease Control, we were able, through long term planning and strategy, to accomplish what no single officer, acting over a one year tenure, could do. In effect, we cleaned house, changing the by-laws and the constitution to limit tenure on boards and committees, so that no one could hold two offices at a policy level nor succeed himself repeatedly, in some instances for ten to twelve years.

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\*Dr. Lennette added this paragraph after completion of the interview process.

Hughes: How were you changing things?

Lennette: We had a publications board on which the chairman would serve in perpetuity. The same thing was true of the meetings board. Well, it got to the point where the staff member in Washington who was working with, let us say, the director of publications, felt he was working for that individual and not for the society. And the individual who was chairman of the board thought he would run things the way he wanted. He didn't care about what the society wanted. He'd do it his way. Well, things were getting really out of hand, and you had all these little fiefdoms. So over a period of years we cleaned the whole house out. We changed the constitution, the bylaws. Nobody could succeed himself in these directorships, whether it be for education, for publication, or for meetings, more than two terms. And you couldn't serve in another office. You couldn't be chairman of publications and be president also.

Hughes: I bet you ruffled some feathers.

Lennette: We ruffled quite a few, and the people who saw what was being done knew it was aimed at them. But it was a united front, and that's how we got it done. It was all to the good. It changed the whole complexion of things. People didn't think that they had a job there forever, that nothing would happen. Somebody was on their back.

Hughes: What would you say are the major goals of the society?

Lennette: To promote the science of microbiology. And for a long time, the virologists were all part of it, and they should be, I think. Well, those in basic virology began to complain that the meetings were too big, and there were too many distractions, and the society didn't give them enough space to hold their meetings. So they were going to start their own society, which they did.

So what happened was all the molecular virology boys got together and formed a new committee that started off this new society, the American Society for Virology. It's two years old now. Well, originally they were going to restrict this to the molecular virologists. We tried to dissuade them. I wrote several letters of dissent. Apparently they later decided, after some thought, that they just didn't have a big enough membership to make this thing go. So they decided to open it up to virologists in other fields--veterinary, medical, agricultural. So it's a fair-sized group now.

But the question is, can they really survive on their own? Because now they're removed from all of the other background science, which I think has always been very helpful. And there is still an unresolved problem, because for some years Thomas

Lennette: Francis at Michigan, Joseph Melnick at Houston, Robert Huebner at Bethesda, Joseph Smadel at Walter Reed, myself, and a few others, tried to get the society to start a journal of virology. The council always came up, "No, we don't need another journal."

Hughes: You're talking about the Society of Microbiology?

Lennette: Yes. We felt we wanted a journal for virologists that would publish everything, epidemiology, basic virology, immunology, you name it. As long as it's got a viral background, we would accept the papers. "No, we don't want that kind of a journal. There are other places you can publish. You've got Infections and Immunity, which is run by the society. You've got the Journal of Clinical Microbiology, which is run by the society."

Well, finally one year the council decided yes, they would establish a journal of virology. And who do you suppose the editorial board was? Everybody who had objected to it before. [laughter]

These were all molecular virologists. So that journal then became a house organ. It became the personal preserve of the molecular virologists. You could not and you still cannot publish a paper in the journal unless it's molecular and very basic. And I raise that question now, if you've got your own society, what are you going to do with this journal? I'm trying to open it up to everybody. I don't know how much success I'll have.

Hughes: What's their answer?

Lennette: Well, they can't answer that. The successor to the previous guy is also a molecular virologist. But his status, and the status of the journal, has to be determined. I have been bitterly opposed to that journal from the beginning because of its attitude toward the others. I said, "You know, these are all paying members. We're all paying our twenty-five or forty dollars a year, whatever it is. And then you deny us the privilege to publish in our own journal."

So when I was vice president, I attended the annual meeting in New Orleans. I attended the meeting of the publications board at which each of the editors-in-chief gave a report of how many papers they had and how many pages were used and what the costs were and profit and loss. The biggest money maker was the Journal of Clinical Microbiology. Which is interesting, too, because for a long time they wouldn't set up a separate division for clinical microbiology. "There's no need for that." When they finally did, they found out it's the biggest division in the society.

Lennette: Anyway, we got around to the editor-in-chief of the virology journal, Dr. Robert Wagner, and he presented his report. He said, "We've got all these wonderful papers. They're magnificent papers. They're real contributions of our knowledge. We just don't have enough pages. We need more pages." It's a recording that we used to hear every year.

I just finally blew my cool and said, "Well now, Dr. Wagner, you've been saying the same thing now for twelve years that I know of, since the journal was founded. You need more pages each year. And every year you report a deficit, and each year it's bigger. This year it's over a hundred thousand dollars. Now so far as I personally am concerned, I think you have several ways in which you can go. Number one, open up the journal to all the virologists, which will then increase your circulation, which you are unwilling to do. Or the other alternative is to fold it up because you're losing money. And the third alternative is do something in which you're going to at least break even and justify your existence."

The audience was stunned. They had never heard anybody put it as bluntly as I did at that meeting. Everybody applauded my saying so. They didn't want to say it themselves, but they wanted me to say it. That's where it stood. And that journal has lost money every year. And it's run by the very people whom they denigrate, the clinical microbiologists. And this is the big chunk of the society which is paying the freight on this journal.

Now, in England Peter Wilde started up the Journal of General Virology. The first issue came out as a skimpy little thing. But I wrote him a letter, and I said I was delighted to see it. I was delighted to hear that he was going to do something that his American counterparts had not done at the time. That journal would take anything dealing with virology, basic or applied.

Hughes: Did he do that as a balance to the Journal of Virology?

Lennette: Well, in a sense, because, you see, he and his colleagues in the Society of General Microbiology, which is the British equivalent of the ASM, felt there was a need for it, so they started this journal. And I told him, that's really what we need--something that would offer its pages to everybody who's got an interest in virology. That thing's like this [indicates the thickness with his hands] now.

Hughes: What about Virology?

- Lennette: That was the first one on the scene. Virology has now become pretty much a plant journal. Medically it's a nonentity.
- Hughes: So you've got a general journal, you've got a molecular biological journal, and you've got a plant virology journal.
- Lennette: That plant virology is also in large part molecular.
- Hughes: If you are going to publish in a virological journal, you're restricted to the Journal of General Virology, aren't you?
- Lennette: Yes, we publish a lot of our papers there. By preference we do.
- Hughes: That's interesting that there's no American journal that will accept papers on all aspects of virology.
- Lennette: Infections and Immunity comes close. Some of our papers go in there. We put some in the Journal of Clinical Microbiology. Some go into the Journal of Immunology. Not so much in Immunology any more. The American Association of Immunologists, with respect to the virologist, has pretty much the same history as the Tissue Culture Association, except that it's much older. The American Association of Immunologists goes back practically to the turn of the century, and some very prestigious people were involved in immunology, like [Karl] Landsteiner.

The Journal of Immunology wasn't doing very well, because the number of immunologists was too small. After World War II the virologists came in because they had to know a certain amount of immunology, and what they did know was kind of a naive immunology, if you follow me. But there were enough virologists to support that journal and support that society. You had to be elected into the society. You just didn't pay your dues and become a member. So I as a virologist am just like any other member, and I was elected to the council and eventually, after about six or seven years, by rotation through the council, became the president.

It was pretty obvious that all of a sudden immunology was going to be a science in its own right. It just exploded, exploded to the point where in a few years I couldn't even understand what was in the journal anymore. Today it's a very esoteric, in-depth kind of a journal. And for most of us, it's no longer a society to which we can belong, because we're paying to belong to a society which we don't understand too well unless you're involved in immunology to any depth.

Hughes: What's going to happen to virology with this schism? You've got two sets of people with very different approaches to the virus. You people with a medical background are--this is a very naive summary--more interested in the effects of the virus, where the molecular biologists are more interested in the virus itself and its submicroscopic composition.

Lennette: That's open to question, too. The medical virologist or the plant pathologist is interested in the virus itself, in the natural history of the virus, what does it do, where does it come from, how does it get into its host, what does it do to its host, why does it do it, and how do you go about negating its action. The molecular virologist doesn't care so much about the virus. He wants to use it as a model for something else, see. He's studying enzymes. He's studying mutation. So he uses the virus as a model.

And this is the kind of stuff, as I think I mentioned several times in the past, being taught in the medical schools. And this is not what the medical student needs. He needs to know how the patient gets infected, what kind of a disease he's got, how you diagnose it, and how you treat it. He doesn't have to know all this esoteric basic virology.

As a matter of fact, I was talking about the New England Journal of Medicine here just a little while ago. It had an article about medicine of the future and how it has to be changed. This was by a professor of medicine at the University of Vermont. Beautifully written article. It says one of the things we have to dispose of in the future is the first two years of medical school, which are entirely passive. Now, this is where a lot of this esoterica is taught. We don't teach pathogenic or medical microbiology anymore. We teach molecular. We don't teach physiological chemistry anymore. We teach biochemistry. And you can do that for every field.

Hughes: What was he proposing?

Lennette: He didn't come out with anything specific, just that we've got to change our outlook on how medicine is practiced. We have to realize that we're coming into a new biotechnical era with computers and everything. You're going to have to depend on computers to do many of the things which are now being done intellectually or mentally. You've got to get the doctor closer to the patient than he has been, and there just isn't enough time to deal with all these other distractions. And he thinks the teaching, the licensing, all has to be changed. Examinations have to be changed. The emphases are all wrong. So there's a big change coming.

Being human, we're all prone to follow fads and fashions and fancies, and that's what's happened to medical education. Everybody had to have a department of medical virology, which was essentially molecular virology. And this isn't what the students need. So the

Lennette: deans were swept in that direction. They had to have one to compete with Burning Stump, Iowa, which has a cow college and which also has to have a molecular virology department. Just a competitive spirit. And it's been overdone.

Hughes: Is that enough about the Society for Microbiology?

Lennette: Yes.

#### The Federation of American Societies for Experimental Biology

Hughes: You were president of the Federation of American Societies for Experimental Biology from 1968 to 1969.

Lennette: That was fairly automatic, because there are seven constituent societies that make up the federation. There are physiologists, biochemists, immunologists, chemotherapeutists, nutritionists, pathologists, and cell biologists.

Hughes: No virologists.

Lennette: No. I'll have to look at the cover. But there are seven constituent societies, with the federation at the top of the pyramid. The president of the federation is also president of one of these constituent societies. It goes by rotation. It goes right down the cover of the front page, starting with the oldest society, in rotation. The year I was president, it was the turn of the American Association of Immunologists, so I automatically became president of the federation.

Hughes: How did the federation grow up?

Lennette: It was put together in 1912 by one individual who felt that there was a lot of effort lost in putting on meetings (he was a physiologist) and putting out journals. Why not try to get a structure which would have a central core of administrative people to do, for example, the publication, the editing, and the redactorial work, and then have a permanent secretary? Each society then would have a secretary stationed in Bethesda--Rockville actually--who would take care of all the matters of the society of which he was a member, like physiology or biochemistry or immunology. Some of these executive secretaries were paid. The poorer societies, like immunology, had a volunteer; it still has a volunteer because it is a small group. I don't know what they're going to do eventually. But the big ones, the wealthy ones, like the physiologists and the biochemists, had pretty good office staff. Just like the ASM.

But here again, the federation is beginning to fragment. It has probably served its purpose, and now the biochemists, over the last ten years I guess, have been pulling away, having their own meetings, and then the others are going to follow suit, I assume, so eventually

Lennette: the federation may just disintegrate. It's a matter of size. When the societies were small, you could have an international conference. When I was a student, the only people who went to an international congress were all the famous scientists. They got together in Budapest or somewhere, and there were maybe a few hundred. That was opened up in NIH days, when grant money became freely available, so that everybody would go, and you would have three thousand people at the biochemistry congress. The people you want to see, you may never see during the course of the meeting. So it's outlived its purpose, I think.

Hughes: The American Association of Immunologists was one of the organizations under this umbrella?

Lennette: Yes.

Hughes: Is there anything particular to say about the American Association of Immunologists?

Lennette: No, except that it's a good, well-functioning organization, and I think it's representative of immunology in this country. But they too have problems of fractionation, because you have people there who are dealing with some very important areas of immunology. For example, genetics, immunogenetics, immunochemistry.

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#### The Armed Forces Epidemiological Board (continued)

Hughes: You were also president of the Armed Forces Epidemiological Board.\* You told me about the decline of the board. It no longer exists, is that not true?

Lennette: No, it still exists. But in my estimate, it's a hybrid. It's a mongrel board. It tries to cover too many areas of medicine, and it no longer has the stature nor the prestige that it used to have. Nor does it serve the function that it used to, which it used to do very well. The board was founded during the war, 1941, I guess, by people like Stanhope Bayne-Jones, who was a brigadier general. He was also professor of microbiology at Yale, a very eminent microbiologist. He became a brigadier general when hostilities developed, or maybe he was in the reserve, I don't know. But he was one of the people instrumental in putting together the board, which drew upon

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\*Dr. Lennette was president from 1973 to 1976.

Lennette: quite a group of distinguished people--Thomas Francis, John Dingle, Colin Macleod, a number of others. I don't know who was on the early board, but I do know they were very distinguished people. They decided what the policy would be epidemiologically, what they should be concerned with. It was mostly infectious disease that they were concerned with, because that has always been the big problem in the military. Still is.

So they then formed commissions, the commission on influenza, commission on respiratory disease, commission on intestinal disease, commission on malaria, and so on. These were all charged with certain areas to keep abreast of developments on a practical basis. The chairmen of these commissions were generally university people within their own departments who had graduate students they could call on. The board would meet once a year and would have before it all the chairmen of the various commissions. And these chairmen would make reports on what had been accomplished by each commission. Each commission had the ability to call on graduate students or on other members of the faculty that could be put into the field in a hurry as a study required. This was a real plus. There was pride in performance. These people could be put together in a unit within twenty-four to forty-eight hours and take off somewhere. That doesn't hold today. And instead of just dealing with infectious disease, they deal with everything now, weight problems, heart disease, and environmental exposure to carcinogens, and all this kind of thing. Now, you can't have a group that's big enough to cover all those areas meaningfully. So it isn't what it used to be.

Hughes: What does it call itself now?

Lennette: Armed Forces Epidemiological Board.

Hughes: Still epidemiology, even though...

Lennette: It doesn't do very much in my estimate.

Hughes: What is its relationship with NIH, if any?

Lennette: None. It served purely the military and primarily the army. The army was the major supporter in terms of finances. And it was the army who ruined the board by saying, "We don't need all these civilians around." This is some ten years ago. "We've got enough talent in the army. We've got all these young fellows coming in. They do their research at Walter Reed. We just don't need these people." They wrote a report on the structure and functions and accomplishments of the Armed Forces Epidemiological Board, written by three in-house officers! Now, you can imagine what kind of report that was. So when we finally got to see the report, we really blew our top because it was so unfair and so one-sided. We just couldn't accept it. In a sense it was a real insult to the people on the board. So it was the military, the preventative medicine department, and within Walter Reed Hospital, who destroyed the board as it was constructed.

Hughes: And you had no recourse at that point?

Lennette: Well, it just went downhill over the next few years. I finally got so disgusted, I resigned.

#### The Wooldridge Committee

Hughes: I notice that you were on the microbiology panel of the Wooldridge Committee [in 1964], which I believe was formed to evaluate the NIH? Is that true?

Lennette: That's so far back, I've forgotten. Yes.

Hughes: It was a White House committee.

Lennette: It was appointed by the President.

Hughes: Do you remember any of the details?

Lennette: I don't remember what all we did. We had to report to Wooldridge. He was part of Thompson, Ramo, Wooldridge--TRW, the big research and development company in Los Angeles. The committee was taking a look at the research programs of NIH.

Hughes: Did this committee produce any repercussions?

Lennette: I don't think there were any real repercussions from the report of this committee.

Hughes: Now, your consultancies are also very numerous. If I mention some, perhaps you could pick out the ones that you think are worth talking about. Communicable Disease Center, the NCI, WHO, the U.S.-Japan Cooperative Medical Science Program.

#### The U.S.-Japan Cooperative Medical Science Program\*

Lennette: The U.S.-Japan Program was one of the bigger ones. This arose in 1965 when Mr. Johnson was in office. The prime minister of Japan, Mr. Sato, and President Johnson were closeted in the White House for about a day and a half or two days. When they emerged from that

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\*Dr. Lennette was a member of the U.S. delegation from 1970 to 1976.

Lennette: meeting, one of the decisions that they had reached was to have a U.S.-Japan Medical Science Program. There were several other programs in addition. This was early in 1965, as I remember, about January or February.

Hughes: Do you know anything about the background?

Lennette: Oh, I suppose it was a goodwill gesture. This was one of the ways of doing it. Subsequently they developed other programs. Similarly with the Soviet Union and Australia and I don't know who else over the years.

The State Department was charged with implementing it. Well, with the ponderous bureaucracy that we have, it just lay around there for three or four months until one day somebody happened to think, "We're reaching the end of the fiscal year. We've got to do something to get this thing moving."

So whoever it was in the State Department--I can't think of his name, he was in charge of scientific affairs--called Jim Shannon at NIH and told him that we ought to get moving on this. Jim said, "It's your baby. What do you want us to do." He said, "We've got to get a budget together and get a few people on this committee here and start a delegation and get some panels going."

So what does Shannon do? He calls in two people, Joe Smadel, who had left Walter Reed Army Institute of Research and was now associate director of NIH, actually working with Jim Shannon at his office, and also Colin MacLeod. Now, Colin had been number two man under Jerome Weisner in the Office of Science and Technology in the Kennedy administration. And he may have been at that time, too. I'm not sure.

So here are these two top echelon people, Joe Smadel and Colin MacLeod--"Do something." So they put together a few prominent figures, like Thomas Francis and a number of other people, to form what they called a delegation which would represent the United States Department of State. It was set up like the Armed Forces Epidemiological Board-- under that you had these various panels.

Well, I got a phone call from Colin MacLeod one day out of the blue saying that they were setting this up and he wanted me to be chairman of the virus panel. I wasn't sure I wanted to do that. I had so many other things. As you can see from my record here, I had a finger in every pie, mostly because I can't say no, I guess.

He said, "We decided, Joe Smadel and I, that you would be the logical person for this. I'm not going to go back and tell Jim that you won't do it."

Lennette: I said, "All right, I'll try it," and a week later, we all got phone calls, "Get back to Washington. We've got to produce a budget." So here's Shannon up at the blackboard in this meeting room. He's the director of the NIH, a huge operation. A terribly busy guy with huge commitments. We had three or four different budgets that we were making up at different levels, and it took us a couple of days to do all of this. As you can imagine, it was cut way down.

So they were going to have a meeting in Honolulu. This is 1965. I still remember, that was the first meeting in Honolulu. It was in the fall, as I remember, sort of an organizational meeting. We had our panels appointed, and we all met there with the Japanese counterparts. It was quite a meeting.

The next year we met in Washington, and we alternated back and forth. Eventually I was appointed to the United States delegation representing the State Department, so I got to sit up there at the table with all the Americans on one side and the Japanese on the other side--just like the U.N.--talking about programs and how to implement them and who should do what and where the support was coming from. It was very interesting. I sort of liked that, because I felt we were making progress. From the standpoint of relations between the countries, I think it served a very good purpose.

Hughes: It no longer exists?

Lennette: Yes, it still exists, but it's very low key. After a few years the program was functioning very well. Although it was a U.S. State Department project, the money went to NIH for funding purposes. And then eventually NIH just sort of absorbed all that money into its own budget. This is what you can't do legally if you're selling real estate. You can't commingle funds. But that's what they did. So they had to support these panels out of their own funds, and, of course, every time there was a cut, the U.S.-Japan Program was cut. But it was a good program.

Consultant to the Communicable Disease Center, Center for Disease Control\*

Hughes: What about your relationship with the Communicable Disease Center?

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\*Dr. Lennette was a consultant from 1950 to 1962.

Lennette: A great deal of that was on rubella. When they were working out the rubella tests to try and standardize them, I got very much involved in that, and then later on in connection with sanitation, water, and viruses. But that was a minor part of the whole thing. It was mostly on rubella vaccine.

#### The World Health Organization

Lennette: With WHO, that went back many years, back to about 1952.\* I still am a consultant at WHO. They haven't called on me the last couple of years because they are being reorganized, too. A whole new coterie of people has come in.

Hughes: What did they expect you to do?

Lennette: In 1952, that's when we were working on Q fever here, and Q fever had turned up in Spain. The Spaniards were concerned about it. They wanted to get some assistance in setting up a program in the laboratory and in the field and how did we do it? So Geneva wrote to me several times and wanted me to come over. I went to Geneva and spent a couple or three days with Dr. [Martin] Kaplan, who was the veterinarian in charge of the Q fever program. Now, at this time the WHO virus unit was housed in just a few small rooms in the old Palais, practically across the street from the new Intercontinental Hotel. Then later they moved to a brand-new building way up at the top of the hill, up near the International Red Cross headquarters. It was a very small operation.

I spent three weeks in Madrid in May. God, it was hot. Fortunately, I left before June when the real heat came in. It was a good exposure to how other people in the world operate. The Spaniards were really laid back. And I'm not so sure that that's all wrong, either. At first I thought the hours were pretty awful, but then I got into that pattern. I had been through this in Argentina and Brazil.

They used to get into the lab around ten o'clock in the morning. They'd be gone at one o'clock, and they wouldn't show up till five. Then they'd leave at seven. And I was trying to run a laboratory. You can't run a laboratory that way. And you can't do field work that way, either. But anyway, I gave them the benefit of what little I knew about Q fever. That was my first assignment.

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\*In 1949 Dr. Lennette became a member, Regional Laboratory, Influenza Study Program, under the aegis of WHO.

Lennette: Then later on I got called in on the enteroviruses and the polio viruses and especially on respiratory viruses, influenza. Then toward the very end I became a consultant also to the East African Virus Research Institute in Uganda, at Entebbe. So that served to tie in the African work along with the work WHO was doing.

On one occasion I spent six weeks travelling down the west coast of Africa, down into South Africa, and then back up the east coast.

WHO said that they had this big program on arthropod-borne viruses, but mostly Congo virus, Congo fever. The three East African states, Tanzania, Kenya and Uganda, had formed a confederation. The money was interchangeable, no customs back and forth, etc. But now it was falling apart. One country wouldn't accept the other's money, and you had to have passports to go back and forth. The collaborative projects that they had with these various countries were also disintegrating, because you couldn't get material in and out of the countries because of the customs barriers. So if you wanted to test specimens, let's say from Zaire, in Entebbe where we had the lab, there was no easy way to get them in. It was difficult.

I started out in Dakar, Senegal, and one of the WHO functionaries, a Czech, stationed in Entebbe, came from Entebbe to meet me in Senegal. He was already there when I got off the plane with my wife. He was there with Yves Robin, a French army colonel and director of the Pasteur Institute. So we spent several days there and then started down the west coast. Stopped at several places, Ghana, for example, and Nigeria. Tried to get the people motivated to get out in the field. "Everything isn't as bad as it's painted. You're going to have a good program. Let's build it back up." Mostly a sales job.

Hughes: Why were the programs so demoralized?

Lennette: Because of the laboratory. The Entebbe laboratory was doing all the laboratory work. See, the East African Research Institute was put together by the East African Community, the three countries. That institute was built, the buildings were erected, by the Rockefeller Foundation just before World War II to study tropical diseases, mostly viral disease. And then when the Rockefeller Foundation pulled out after the war, the British took over. Then when Uganda became separate, they gave it to Uganda to operate. So they had the East African Virus Research Institute. It wasn't Ugandan. It was East African, the three countries.

They had a very nice, well-equipped laboratory. Then WHO got some money from the Wellcome Trust in England, and put up a beautiful laboratory right next door, which was then part of the East African complex, although it was staffed and paid for by WHO. So that's why all the material was supposed to be sent to Entebbe.

Lennette: From there Elizabeth, my wife, and I went on down the coast. We stopped off in Zaire and then on down to South Africa, mostly to talk to the people who had been doing work on polio. By that time we had left our Czech companion in the Central African Republic. He couldn't get in and out--there was one plane a week in, one plane a week out. And we just missed one, so we had to stay in Zaire a whole week to get the guy coming back again. It was a pretty dreadful experience for him, because he was a Czech and had a Czech passport as well as his own U.N. laissez-passer. He had a hard time, but he finally was able to get out of the Central African Republic and got across the country to the east coast, ending up in Entebbe, his base. We stopped in South Africa and Zambia, and then went on to Kenya. Here I am; I got everybody gung-ho, ready to operate.

We got up to Salisbury and got a plane out of there for Nairobi. It was a Sunday. We got into Nairobi in the middle of the afternoon and by the time we got to the hotel, it was practically dinner time. First I asked for the mail. Well, they pulled out some mail. I said, "There aren't any telegrams or anything?" "No, nothing. This is all." I said, "Are you sure that's all?" "Yes." No word from Entebbe. So we went to our room to freshen up and came down to have dinner. Just about the time I was walking into the dining room, I'm paged. So I listen in disbelief, I said, "Who's going to page me in the middle of Africa, in Nairobi?" It was Entebbe calling. And it was my Czech colleague on the phone. He said, "Don't come to Entebbe." I was scheduled to leave the next morning at seven o'clock and then come back on the seven o'clock flight in the evening, and the following morning Elizabeth and I were going to depart for Addis Ababa to see the rabies operation up there. So he said, "Don't come." Don't come? I didn't think I was understanding him because of his English. So he finally got off the line and got a Nigerian, Tunji [O. A. Fayinka], who subsequently spent six months in our lab here, to talk to me. Tunji said, "You can't come. Geneva cancelled your orders." That was kind of strange.

Well, on Monday morning I went down to the U.N. office, which was primarily the agricultural office, and met a surly U.N. functionary there, who asked, "Doctor, don't you ever listen to the radio?"

I said, "No." Everything I had been reading in the papers, Uganda's fine. There were no problems.

He said, "Mr. Amin was on the radio Friday night and said that if he gets any evidence that the United States is supporting the Israelis"--that's when they were having their difficulties with the Israelis--"is supporting, giving aid and comfort and supporting the Israelis, I'm going to incarcerate them all, beginning with the charge d'affaires." The ambassador was already gone, back in the states for consultation.

Lennette: Here I would have walked right into this hornet's nest. They didn't have any orders to cancel--they were just telling me to stay away. So that ruined the whole thing, because Entebbe was the linchpin; we were building everything around the Entebbe laboratory. Now, all of a sudden we can't get in there. Amin is acting up. It was pretty dreadful. We had no choice. I just stayed in Nairobi that day and then went up to Addis Ababa and Geneva, and then on home. But all I got out of that trip was six weeks of sightseeing and disappointment with not being able to nail down what we originally set out to do.

#### The National Cancer Institute

Hughes: The last association to discuss is the National Cancer Institute.\* Did that have anything to do with the big cancer grant that the lab had?

Lennette: Yes. We were involved in the virus part of the cancer studies. We weren't concerned with the epidemiology or the veterinary portion or the chemical portion. Most of our contacts were with Dr. Huebner and his group at the National Cancer Institute, NIH, who were working on the oncogene theory at that time and also studying the transmissibility of various animal cancers, such as feline leukemia, for example, and what happens to people who are exposed to leukemic cats.

In effect, the laboratory subsequently became sort of a collaborative arm of Huebner's operation. He was a remarkable person. He never remained very long in Bethesda, except to mend his political and financial fences, then he'd take off and see all of these people he had working with him all around the country, and in Europe, too, for that matter. His knowledge of the cancer virus field and other parts of the cancer field was just enormous. Very remarkable person.

He would come out here periodically, and we'd sit around a table in the Virus Lab library and outline a program, what we thought ought to be done. Well, we'd do this part and somebody else will do the other part, like a subassembly line. Everybody was doing a piece of the action. It worked out very well.

Hughes: I was wondering your opinion of the concept of very specifically targeted research as embodied in the National Cancer Act?

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\*Dr. Lennette was a member, Solid Tumor Virus Segment, Special Virus Cancer Program, from 1966 to 1972. He served as a consultant to NCI from 1967 to 1973.

Lennette: I think specifically targeted research is fine if it doesn't become your main aim. I think there are certain things you need done, that have to be done or should be done, and the only way you're going to get them done is to get adequate funds and say, "Look, we need somebody to do this." And then get somebody to do it.

In large part, that has been beneath the dignity of academia. Most people want complete freedom. Just give us the money and don't bother us. Go away until we need some more, then just come back and give us another hatful. That's been the attitude. That perforce has changed, of course, in recent years.

I don't have any objection to targeted research provided you have the major part of your funds in free research, because after all, money for basic research is really money in the bank. It's what you eventually develop that's the interest. It pays off if you use all this information.

Hughes: But I thought NIH would discourage just that sort of freewheeling research, which, when you look through history, is what has been most fruitful. You as a researcher would probably admit that often the most significant findings of any given piece of research you didn't expect when you started the project.

Lennette: Sure. Serendipity.

Hughes: Right. To put such emphasis on finding the cause of cancer, doesn't that distort the notion of research for knowledge's sake?

Lennette: No, it was broader than that actually, because that used to be some of our objections to this. To find the cause of cancer, we have to determine what determines growth, how do you control growth. That's wide open for all kinds of basic research. It's all-encompassing. But there are certain things--a new drug somebody is trying, some chemical, some therapeutic agent in animals, and it seems to be pretty good--then you've got to have it in man. That's the payoff. What it does in monkeys is one thing; what it does in man is something else. You've got to find people competent to do these trials. So you just sort of advertise and say that we've got this... Well, most people who know the literature know that this thing is working in animals, and are they interested in doing it in man?

But I'm unhappy to see some of the trends at the present time with the National Institute of Allergy and Infectious Disease (NIAID). For some years I tried, beginning in study sections, and later on at various committee meetings, to get them interested in some very prosaic things. Number one, we have a lot of diseases we think are of viral origin, but we can't get the virus out. What we need is information on susceptibility of a whole new series of cells, shrimp cells or whatever, and find out how susceptible they are to these various agents. Nobody would put five cents into that. That's too prosaic. Nothing intellectually stimulating about that, of course not, but it's something that needs to be done.

Lennette: The other is viral diagnostics, which we've been doing for years in this lab. I've been trying to get NIAID to put some money into the development of the diagnostic armamentarium--better methods for isolating viruses, better methods for doing serologic tests. Get some laboratories with this interest and support them; give them a free hand.

No way would the council or the study sections listen to that. Now all of a sudden, when you pick up the yellow sheets, they're looking for people to do the very things mentioned here. But what I object to is this now has become directed research out of NIAID. When they issue a proposal--we want you to do A, B, C, D, E and F--and you have no chance to think; you just do it automatically, then I think that's wrong.

The other is allocation of huge blocks of money to one or two institutions to do something like this. We will establish an influenza study center in two different universities, and you people do all the influenza research work.

Hughes: You mean literally all the work?

Lennette: Yes. Well, you don't have any institution big enough to do all the basic research, to do epidemiology, to do a lot of immunology. You're putting all your eggs in that one basket, and if anything goes wrong, you've had it.

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NIAID decided the program, who would do what, and take a piece of the action. But I don't think that splitting up these grants is really the way to go. All your money is tied up that way in two institutions. I think you've got to have more support for a broad and diversified program. Well, the excuse for that is funds are limited. Sure they're limited. But how do you want us to use them? Is this the way to go? I'm not so sure it is.

Hughes: The last questions are on some of the significant names in virology that we've mentioned in passing. In fact, a few of the people on my list I think we haven't mentioned at all.

Maurice Hilleman

Hughes: The name Maurice Hilleman arose in my conversation with David Lennette yesterday. He said not only was he a very colorful character in his own right, but he had quite a bit to do with getting Merck into biologicals and vaccines.

Lennette: Hilleman was one of Joe Smadel's proteges, very bright. I think that when Merck gave him the appointment as director of research in the biological field, cell biology, they did a very smart thing, because he's a very capable person. He knows a lot of people in research and industry. He knows virology. He knows cell biology. He's got both feet on the ground, or, as they used to say, his head is screwed on right, and he's just a highly competent person with very little use for people who don't measure up to his standards. So he's been pretty ruthless in hiring and firing people, and thus he's built up a very competent staff.

Furthermore, his early track record, I guess, impressed the hierarchy of Merck, Sharpe and Dohme, that whatever money he got, he spent wisely and with a good return. So he put together a team which was ready to go at any instant. For example, if there was a new development in recombinant DNA techniques, he didn't have to scout around and try to hire a dozen people over the next six months and be the last horse in the race. If anything broke that was at all propitious or looked like it might be a good way to go, he was there. He had the team. All he had to do was just get out of bed the next morning and say this is what we're going to do, and they did it. He's a remarkable person. It's going to be a long time before they find somebody else like him.

Hughes: Does his colorfulness relate to his outspokenness?

Lennette: Yes. Some of his language is occasionally fairly lurid.

Hughes: Can you talk about the drug companies and their relationship with biologicals and vaccines? You said in the early days it was very difficult to get material for biological research.

Lennette: It still is.

Hughes: Which have been the companies that have been most responsive to this need? And why?

Lennette: They have been responsive only because there's a dollar sign on it.

Hughes: And that's these diagnostic kits that you were talking about?

Lennette: Yes. When there was no dollar sign that they could see, they were not one iota interested.

Hughes: Including Merck?

Lennette: Including Merck and including Lederle. Lederle tried a little bit to make some reagents. They never got very far. Their heart wasn't in it. And I think either Abbott or Parke-Davis prepared some. But it didn't amount to much. So any laboratory that wanted to do viral diagnostic work, like this one, had to prepare its own reagents. For years we grew all of our own viruses and we made all of our own antisera and other reagents, too.

Lennette: Now, when hepatitis came on the scene, and a technique was developed for detecting the hepatitis B antigen with radioimmunoassay, everybody jumped into the act and started making kits. Abbott's been the first in the field. They've got virtually the entire market on hepatitis kits. But there are other kits that have come along for rubella. Now they've got one coming out for rotaviruses. They've got kits for cytomegalovirus. They've got kits for the herpes viruses.

Now, these are diseases in which you get a large volume of material. There are millions of cases of hepatitis, and I don't have to say anything about genital herpes. You're aware from the daily newspapers what the situation is. Well, gee, everybody sees the dollar sign up there ahead of them. They're all making kits. So when you go around to a hospital or you try to get information on various hospitals, whether they do virology: "Oh, sure, we have a virus laboratory." Now, you just delve a little bit deeper and you find, what does their virus lab consist of? Hepatitis, cytomegalovirus, rubella, the two herpes viruses, and that's it. That's where the dollars are. Anything else, "No, we're not interested." No money. So of course the manufacturers like Abbott and Syntex aren't going to make reagents for something which is not highly profitable because of relatively low demand. If this were a disease, they would call it an orphan disease.

These are orphan viruses. Except orphan viruses have another connotation. Nobody is interested in making the reagents. So the situation hasn't improved all that much.

Edward C. Pickels

Hughes: Did you have any contact at the Rockefeller with [Edward C.] Pickels?

Lennette: Yes. He's a very good friend of ours.

Hughes: Could you say something about him?

Lennette: He worked on the ultracentrifuge as a graduate student in physics at the University of Virginia, as I recall.

Hughes: Mid-thirties, something like that?

Lennette: Yes, with a chap by the name of Beams, who was a physicist, and the professor under whom he did his Ph.D. thesis research.

Hughes: Oh, Jesse Beams?

Lennette: I don't know what the first name is. They worked together on this centrifuge. With his background, when Ed got his degree he was appointed to the staff of the Rockefeller Foundation because of their interest. He was very well trained, a very good mathematician, a very good physicist. So he and the chief of the International Health Division Laboratory, Johannes Bauer, worked on the centrifuge together. Pickels seriously, Bauer as a dilettante. When they had nothing to do, they used to go down to the basement and make screwdrivers out of cast aluminum and that sort of thing, because they just love to run those lather.

But he was responsible for really developing that instrument. He had to develop rotors which would stand the stresses of these high speeds. We're talking about fifty, sixty, seventy thousand rpm. These things sometimes just got elongated by the centrifugal stresses at high speeds, and once in a while would just shatter, or the piano wire on which they were suspended would give way. These rotors were air-driven by compressed air. There were slots in the rotor, and this would be driven around by air pressure. When they used piano wire, to get to those speeds they had to have a vacuum inside the chamber so that the air-driven turbine was on the top of the centrifuge. Later on they developed an electrical direct drive. So he was responsible for developing a pretty good centrifuge, which we used in New York. Because of the hazard, however, there was always a brick wall built around the instrument because if it ever shattered, the rotor would either shatter and go horizontally or, more likely, up to the floor above. We had occasional accidents.

Hughes: That must have had a tremendous impact on research of all kinds.

Lennette: It did. It furthered a lot of the research. There were a couple of entrepreneurs out here in San Bruno, who ran a glassblowing and custom-made instrument operation named Spinco. They interested Pickels in coming out to join them. He came here in early 1946 to work with these people and to build centrifuges in a garage down in Palo Alto. They had enough money to build the first one. They sold that, and they built a second and a third and so on. And that developed into a big operation, and eventually they sold out to Beckman. So it became Beckman-Spinco. And by that time he had developed a direct drive and everything. It was a quite different instrument. You see them today; they're nothing like the very primitive ones that we had in New York, or even here as a matter of fact. We still have one of his earliest preparative centrifuges. I think it's machine number eight, produced in 1951. It still operates with no problems today (1983).

Hughes: Did virology immediately seize upon the ultracentrifuge?

Lennette: Oh, sure. That's what they needed, especially the big ultracentrifuge because that permitted you to separate molecules by size.

Hughes: Electrophoresis preceded the ultracentrifuge?

Lennette: Yes, electrophoresis was already in use.

Hughes: So you at least had that way of separating molecules?

Lennette: Yes, but it wasn't very practical. The ultracentrifuge would separate well enough that you could take a substance, and you could determine its molecular weight just by sedimentation patterns and characteristics.

Hughes: I can't imagine how you did research before it, to tell the truth.

Lennette: Well, it opened up new vistas. That was a very distinct step forward, just like the electron microscope.

Hughes: I have more names here. All of these I think we've talked about in passing, but if there's any one of them that you feel that you would like to say a little more about, please do so--Salk, Huebner, Sabin, Horsfall, Hirst.

Frank L. Horsfall

Lennette: Horsfall was my immediate superior when I came on the staff of the Rockefeller Foundation. Very knowledgeable. Very astute. Good scientist. Good thinker. A little aloof. Difficult to approach. I was never quite sure why he was difficult.

Hughes: He was that way with everybody?

Lennette: Yes. He and I got along quite well. We worked on a number of projects together, and then I was assigned to Brazil, because some of staff was coming up on leave or were being reassigned. So my next duty assignment in 1941 was to Brazil, to the Yellow Fever Service. About that time George Hirst came on the staff to work with Horsfall. Frank and I were very much immersed in working on an influenza vaccine. We were on the wrong track, but we were working hard anyway. So when George came on we discussed some of the problems, and Frank decided maybe we ought to have George work on this business of the red cells agglutinating. Every time you cut a blood vessel in these infected eggs, all these damn cells would agglutinate and fall out, and you practically would lose virus. Well, we were too busy, so we gave George the assignment, and as I said earlier, he studied this phenomenon very thoroughly, being the good scientist that he was.

Lennette: Virology was a whole new field to him. He had been working on streptococci before that, with Homer Swift at the Rockefeller Institute. This was a whole new ball game to him, but it didn't deter him. He sat down and really studied it, and got all the details in depth, and described the hemagglutination phenomenon as an assay method.

So we had a new viral assay procedure, antibody assay procedure, too. Well, like everything else, all of a sudden we got a new tool, we threw away all the old ones. And so the complementfixation test was thrown out the window, to the extent that there were only two laboratories in the whole country that were using the complementfixation test. That was myself here in Berkeley later on, and Werner Henle in Philadelphia. The rest of the people used hemagglutination.

And then they found out that the serums contained all kinds of inhibitors. So the results you were getting with human sera in the hemagglutinationinhibition tests had to be tempered by the fact you have to get rid of all the inhibitors. It took us some years to learn what these inhibitors were. But hemagglutination became the standard test. Still is pretty much for influenza and some of the other hemagglutinating viruses. Of course we now have a whole new armamentarium.

Anyway, George later left the foundation to become director of the New York City Public Health Research Institute, which was supported by VD [venereal disease] money. He built that into a pretty good research organization. However, it had very little to do with public health, although it was great for molecular virology. And that's where he made his reputation as a fine and outstanding basic scientist, because he studied the genetics and molecular virology of influenza virus. Did some very, very nice work.

#### Jonas Salk and Albert Sabin

Hughes: How about Salk and Sabin?

Lennette: Well, Sabin had been working on polio for years before Salk ever came into the field. Sabin started working on polio way back in the thirties when he worked under Peter Olitsky, and with Jerome Syverton, Herald Cox and that group. They worked on the encephalitidies, and then they got involved in polio. So most of his career has been on poliomyelitis, although he has also worked on other agents. He has worked on dengue and St. Louis encephalitis and Japanese B encephalitis.

Lennette: When Salk came into the field, he just came in more or less by indirection and happenstance. He was at the University Michigan with Thomas Francis. Francis had him as a graduate student at NYU and brought him to Michigan with him. At Michigan Salk was working on flu. He was doing all of these viral inactivations and comparisons, taking maybe twenty or twenty-five different new strains of influenza virus and comparing them for their antigenicity and inactivation characteristics, and then inoculating them into people to see what kind of antibody response they would give, to pick the best possible strain to put into a vaccine. When he left to go on his own, he went to the University of Pittsburgh. He just happened to be the right person at the right time and in the right place.

When the money became available, following the demonstration that there were the three known types of polio virus, he was in, because now you have to make a vaccine against three different viruses. We can grow them because Enders and his associates, Tom Weller and Fred Robbins, had devised a technique of tissue culture methodology whereby one tissue culture tube is now equivalent to one monkey. Salk had a menstuum which was absolutely crystal clear, yet contained a lot of virus and could be readily inactivated. With his extensive background in inactivating and treating influenza virus, he just went right down the road to develop that inactivated polio vaccine. And that's where matters stood when they set up the field trials. Francis then, as his mentor, became the director of the field trials, and it was quite an operation.

Sabin in the meantime had been working on an attenuated live virus vaccine. His efforts were all sidetracked by the National Foundation for Infantile Paralysis, which put all of its money on one horse, and Salk was the horse they were betting on. So anything that Albert got was just secondary amounts of money or the leavings. He never got all the money that he wanted or really needed.

So the question still has never been resolved, which vaccine are you going to use, the dead vaccine or the live vaccine? We don't have any cases of poliomyelitis, wild polio virus, occurring in this country. You get several cases of poliomyelitis, paralytic polio--this is in adults--as a consequence of the Sabin vaccine, which is known to be hazardous, whereas with the Salk vaccine you don't have that problem. But you can't get it because it's made mostly in Canada and there isn't enough of it being made. I guess the way to go would be to immunize older people with a course of Salk vaccine and then give them the live vaccine to implement their tissue immunity. But you'll never get the two principals together to agree on anything.

Hughes: What are their personalities like?

Lennette: Oh...Sabin is very acerbic, very brusque, very outspoken. He can decimate you. He can wilt you with just a few words. He has an excellent command of the language. He uses it. And there's never any question in his view about his being right. And invariably he is. Well, he has another side to him also. If you're a young student, or a young postdoc starting out, and you're giving a paper, and nobody is making any comments, or if somebody is attacking you, he'll come to your rescue. He'll open up the discussion by making some comment or other to start things rolling. He feels a duty to this young person. "He's prepared this paper. He's come all the way to the meeting. He's giving it and nobody is going to ask him questions." It's kind of demeaning to be so received. Or if somebody is attacking this young person, Albert will step in and defend him. But once you've got yourself a reputation or recognition because you've published some papers, you're on your own. He's right there in the forefront of the pack. If you're not on safe ground scientifically, he'll take you right apart.

That's the way things used to be in the old days. It wasn't all this nicey-nicey business that you see in meetings today. They used to be knockdown drag out fights in those days, beginning with Thomas Rivers. He'd get up to start the assault, and then you'd be attacked by Albert, and you'd be attacked by somebody else, and, boy, you were looking for a hole to crawl into. That's the way the British still do it today. They haven't lost that knack. It's all friendly.

Hughes: What about Salk?

Lennette: Salk is pretty positive about things. He isn't quite as emphatic as Sabin in my estimate, about things. And he's never unsure of himself.

Hughes: Do you have any more comments about personalities?

Lennette: No, I don't think so. I think all the scientists that I've worked with have been pretty remarkable people in terms of their scientific ability. They have not always been the most gentle people, kindest people in dealing with their colleagues or their staffs, and so on. And some of them, I guess, have gotten to the top of the ladder by stepping over bodies. But you find that in any field. There are rascals in every profession, and scientists are no different in this respect of fighting their way to the top and even using their claws if necessary.

Dr. Lennette's Scientific Contributions

Hughes: One last question. What would you consider to be your most important contributions to science?

Lennette: [laughs] I don't think I've made any important contributions.

Hughes: Oh, come on.

Lennette: I made lots of them, but I don't know that any are important. I think I've contributed in building this laboratory and putting together a staff which has done a creditable job of advancing diagnostic virology, together with the large number of people we've trained from all over the world. We've taken in not only students, we've taken in not only Americans, but we've taken in postdoctoral students. We've taken in well-established investigators who wanted to learn things--Japanese, Europeans, South Americans. Over the years we've trained several hundred people.

Hughes: Yes. Well, Dr. Lennette, we'll end there. Thank you very much.

## IV ADDENDUM I

[Interview 9: November 13, 1986]##

Q Fever

Hughes: I think the last time we talked was sometime early in 1983, so I think we should catch up on a few topics. In rereading what you had said about Q fever, there were some questions that occurred to me, and perhaps you have more to add on that subject. Perhaps we should emphasize the multidisciplinary nature of the Q fever research. Was that a bit unusual for that period, which was the late 1940s, early 1950s?

Lennette: Yes, it was unusual, because we used a team. Our own rickettsial part was done by the laboratory staff and I was to head up the project on Q fever, and to this end, the department seconded several people to me. One came out of the Bureau of Vector Control--that was Hartwell Welch--and William Clark came out of the Infectious Disease Bureau, and the additional person was a veterinarian whom I pick up by the name of Francis Abinanti. He came to us from the State Department of Agriculture and was enlisted to do field work. The fourth person was Mary Romer who came from CDC, and was the nurse epidemiologist. We were headquartered here in Berkeley at 1392 University Avenue, the old and original Virus Lab.

A separate team had been set up by Dr. Robert J. Huebner in Los Angeles. He was sent there by the National Institute of Allergy and Infectious Disease to study Q fever, which actually was discovered in Artesia by Charley Shephard. I think we've gone over some of the early history of it.

Hughes: Yes, we've pretty much covered the history.

Lennette: So the project was built on the observation that Q fever was associated with dairy cattle. We were sure, because so many cattle were involved in the southern California episode, that we would run into the same thing in northern California. But as I think we've recorded, we didn't find this to be a problem in cattle here.

Lennette: It was a problem in sheep from the standpoint of the sheep and goats harboring the rickettsiae--not the production of disease in those species. This was quite different from what was encountered in southern California. This is a reflection of the difference in animal husbandry amongst dairy cattle in the Los Angeles area and elsewhere in the state.

A considerable amount of work was done in England, and much of the work that we had done here was confirmed in England, although, if you read the British literature, you would think that the whole thing was invented there.

Hughes: What institution was involved?

Lennette: This came from Cambridge. Very little mention was made of the American work which antedated that, which was a little surprising. Much of the literature would lead you to believe that all the original work on the epidemiology in sheep and goats and the transmission of disease had been done in Britain.

But that's water under the bridge, because with the passage of years, all the original work that has been widely quoted disappears; a lot of that is just taken as a basic truth, a "given," nobody gets credit, because otherwise you would have a list of references which would be incredibly long.

But the culmination of all that work was that Q fever was recognized to be a widespread problem in the States. And in recent years, it has gained more attention and is being subsidized by grants, much of it by the Department of Agriculture. So we have the problem in the States, but we don't pay too much attention to it because diagnosis of Q fever in man is so seldom made by the laboratories. They don't pay too much attention to these rickettsial agents.

It's an unusual thing--it's like an orphan disease, you know. The federal government is subsidizing the so-called orphan drugs. There aren't too many cases of disease, so no one wants to develop a drug to treat a disease which isn't very prevalent. And industry volume being what it is, unless there's a hundred million dollar market, they won't touch it. They don't want to make a mere two or three or four million. Q fever would fall into that category. As a matter of fact, the Q fever antigen for diagnosis has not been produced in this country. It has come either from Australia or from England.

Hughes: Again, for monetary reasons?

Lennette: I guess for monetary reasons. And so the people here in the laboratories who are interested in doing Q fever diagnosis have a problem, because they have to import this material, and when it arrives on the scene here in San Francisco or anywhere else in the country, you spend the day with the customs people, trying to get it cleared. So it's very disconcerting to import it from either country and have to go through all this red tape.

However, that's being taken care of now, because Virion, a Swiss company, is producing a complement-fixing antigen which is cleared by the Food and Drug Administration for sale in the States, and this is kept in the Virion distribution center in Morristown, New Jersey. So people can just order it directly from New Jersey.

Hughes: Who was responsible for gathering that original multidisciplinary team?

Lennette: I was.

Hughes: How did you go about doing that?

Lennette: Well, I had been in the Department of Public Health before because I was assigned here to Berkeley by the Rockefeller Foundation in 1944, and I was here until 1946 and then went back East. When I came back here in 1947, I came primarily because I wanted to work on Q fever, which was a new disease--it was kind of a fad, I guess.

So when I came here, I knew some of the people who were involved, except for the veterinarian. I wanted Hartwell Welch to work with us, and I wanted Bill Clark to be part of the team. And the department did it very well because they seconded these people, and these people then were responsible to me and not to their own units, which made life much simpler.

Hughes: Was the southern California team assembled in a similar fashion?

Lennette: Well, they brought some of their people from Washington, but they used some of our people from here, for example Dorothy Beck, who was in the Bureau of Acute Infectious Diseases. Dorothy Beck was the epidemiologist. She was seconded to work with Huebner. He also originally, I think, had Hartwell Welch. And then he had a veterinarian by the name of John Winn who was a CDC staff member. He was seconded to work with Huebner. And there were one or two other people I don't recall. Joseph Bell I think also did some work with Huebner. He was from NIH. Oh, yes, there was also Bill Jellison, of the Rocky Mountain Spotted Fever Lab. He was on the team as an entomologist.

Hughes: What was the relationship between the two teams?

Lennette: Between Huebner's team and our team?

Hughes: Yes.

Lennette: At first it was a little--[pauses] what shall I say--

Hughes: Strained?

Lennette: A little strained, yes, because Huebner had come on the scene and had taken over southern California, and he was doing a good job. He started out doing a lot of serology on cattle. Well, of course, when we started out operation, the first thing we did was look at cattle too, which was a reasonable thing to do. However, serologically, our cattle up here in the north were essentially negative. He would find, oh, eighty or eighty-five or ninety percent of a herd to be infected. We would find maybe one or two percent. So he accused us of not knowing how to do complement fixation tests. And I reminded him that I was doing these when he was still in short trousers, so you can see we got off to a poor start.

However, that was resolved in about a year or so, and we became very good friends. He was a remarkable person, actually, especially when he got into the cancer field, cancer virology. He had so many irons in the fire all over the world it's unbelievable how well he kept up with his various collaborators. He was just bubbling over with ideas.

We later collaborated with his group on cancer epidemiology and cancer etiology--four or five or six years, I guess.

Hughes: When the big cancer prohect came up?

Lennette: When it was the fad to look into viruses as a cause of cancer.

As you are well aware, over the years there've been many, many fads. And it happens in every field, I suppose. A while back, viral hepatitis was the big thing. Everybody had to jump on the hepatitis bandwagon. Pretty soon came herpes. So everybody was abandoning hepatitis to get on the herpes bandwagon. The same with rubella and sexually transmitted diseases--the viral etiology. And then along came AIDS. Everybody abandoned the other diseases and got into AIDS, or into chlamydia, all with high-volume lab testing. Fads and fashions come and go. And Heubner kind of followed trends too, because he started out working on the adenoviruses. From there he went into coxsackie viruses, and then to Q fever. In fact, Huebner really made his mark in his first study by discovering the cause of rickettsial pox and outlining its epidemiology.

Hughes: In talking to your son David, he pointed out that, in his opinion anyway, the Q fever work produced a series of small discoveries. Would you look at it that way?

Lennette: Well, there were a lot of observations made. For example, Clark and I. Together with Oscar Railsback and his people at the Woodland Clinic in Yolo County--which was right in the area where we were doing all of our field studies--reported something like seventy-five or eighty cases of Q fever from a clinical standpoint. We summarized all these clinical observations, but, in effect, we added very little that was new because no matter what we did, we found that Derrick had already done it, except that he didn't have the numbers.

For example, we found that quite often Q fever manifested itself as a liver disease. Many of these people had involvement of the liver. If you go back and read Derrick's early papers, you'll find that he mentioned that, too. And it was sort of maddening, because everything we thought was new, when we went back and searched through the literature, Derrick had already done it. He did his studies very thoroughly. He was quite a person. He spent some time here with us on one occasion, a most enjoyable visit for all of our team.

Hughes: Now, he was the Australian?

Lennette: He was the Australian who ran across this strange disease which he labeled Q fever. It occurred in abattoirs, a strange disease whose etiology he couldn't fathom, so he called it "Q" for query, and not Q for Queensland as is stated in some textbooks. He showed that it was an airborne disease, and it could infect people who had little or no contact with animals per se.

Hughes: Did Q fever represent the end of a certain style of research at the Virus Lab? I'm thinking of the Virus Lab's massive cancer project. Was there a difference in the way you pursued Q fever research and cancer research from an organizational standpoint?

Lennette: Yes. Because in the Q fever research we had our own unit. Well, it was a package. We had epidemiology; we had epizootology; we had the laboratory aspects; we had the vector aspects. So each of these areas was covered by one or more people. So the team in itself was comprised of half a dozen people--professional people along with the necessary laboratory support.

That had happened in the past, but it wasn't too common because it took so much money to set up a team like this. Of course at that time [1950s] the National Institutes of Health were pretty well subsidized--they could do these things, as witness the work that came out of Dr. Chanock's laboratory. If something came along that seemed to be important, they could just direct all of their efforts and energy into a given area. People in academia or in the

Lennette: health department just didn't have that kind of clout or latitude. So we were working on nickels and dimes originally, compared to what they were spending at NIH, until we got Q fever support. I'm not saying this is not the way to do things; I'm just saying this is what happened. These people at NIH had the money and they could do it. There was a certain amount of envy on our part that we couldn't do it.

### Cancer Research

Lennette: But when you got into the cancer area that was a different thing because so much of that was clinical. We were looking for possible viral agents, which was sort of a thankless task. But out of that, they did find in some of these tumors part of the genome represented also in the viruses. And this gave rise to the oncogene theory of cancer. This was described by Huebner and his associate George Todaro.

Many people looked askance at this theory, especially those who thought that cancer was due to chemical agents. And Huebner explained some of this by saying, well, the genes were there, and all you had to do was activate them or get them to express themselves and you would have a cancer. This could be done by chemicals or physical agents such as x-rays or sunlight or whatever. And the theory was kept alive for a long time. Now it's coming to fruition because people are finding these agents or evidence of these agents.

You can go into a whole philosophical discussion of the evolution of viruses, and how they transferred from perhaps animals to man. As you know, one of the theories of what is a virus back in the thirties was the virus might be a piece of a gene broken off in the cell and was able to replicate on its own and in some cases cause disease. There was no proof of that; this was just hypothesizing. However, we do have evidence today that this is quite possibly true. As a matter of fact, there are any number of genomic fragments within the cell that could possibly serve as viruses. For example, the latest ones are introns and transposons

Well, we got diverted here, but what I wanted to point out is the fact that a lot of things get into the cell. There's no reason why viruses wouldn't be transmitted between species. Now, this in itself was not accepted because everything was thought to be species-specific. But I, in a speech, oh ten to twelve years ago, in several places spoke about this matter, that I thought that viruses could well be an evolutionary mechanism for transferring

Lennette: genes between species. This was not original with me. But there was evidence that this could be so, and that this would have to be something that would happen rapidly and over a wide span. For example, development of the skeleton. Why did it develop suddenly in so many different species of animals? There must have been some kind of a crossing of the genes which would give rise to the skeleton. And there are other instances like that.

Hughes: It would do a lot to explain some of the puzzles of the Darwinian theory, wouldn't it?

Lennette: Margulis' work, Origin of Eukaryotic Cells, raises the question of how these observations that Darwin originally made should be interpreted. There are other factors coming into play. I'm not saying that the fundamentalists have the answer, but I'm saying that there might be other mechanisms which up to this stage we have not brought in because we were not aware of them. Margulis has done a real service by synthesizing all of the information. To cover as broad a subject as she did in as great depth as she did is, I think, a remarkable feat. You just can't deny that.

Nathalie Schmidt

Hughes: Well, shall we move on to Nathalie Schmidt?

Lennette: Okay.

Hughes: I'm interested in what research she was particularly noted for, and also your interrelationship because I believe you were scientific associates for many a year.

Lennette: Well, as your record will show, I came back to Berkeley at the end of 1947, and worked on Q fever '48, '49, '50--I don't know--a couple of years beyond that. But at the same time, I maintained my interest in poliomyelitis, and I was seeing polio patients on the infectious disease service at Highland Hospital. From many of these patients I arranged to obtain blood specimens which I preserved over the years on the assumption that sooner or later we, or somebody else, would develop a diagnostic test for polio. Whenever you had an outbreak of poliomyelitis, there were a lot of nondescript cases of central nervous system illness occurring which were labelled nonparalytic poliomyelitis. In another year, you might see a high incidence of the same type of CNS [central nervous system] disease, which previously had been called nonparalytic polio. So the question was, what is this "wastebasket" that we called nonparalytic polio? If we had diagnostic tests, we could resolve some of these questions. Well, about that time, Jordi Casals and others were developing a test for St. Louis encephalitis and for western equine encephalitis. I felt we could develop a complement fixation test for polio.

Lennette: Now, in 1953, the American Society for Microbiology met in San Francisco, and Nathalie Schmidt came out to the meetings. She had just received her doctoral degree under Dr. Harry Harding at Northwestern University in Chicago. She spent that year, from 1953 to 1954, at the Evanston Hospital.

Now, she was out here in 1953 and gave a paper on the serology of psittacosis. As I always have done with young investigators whenever they are new to the field and they are presenting their papers and they're getting a little experience on how to stand up before an audience, I always tell them not to worry, not to get concerned if there are any questions that are asked that they can't handle, that I will take care of them, not to get panicky. And I told her the same thing.

Well, as it turned out, she did a beautiful job and she didn't need any support, and I was quite impressed. So six to nine months later, these polio field trials were coming up and we decided we would do some work on the CF [complement fixation] test. I offered Nathalie a position on the staff and she accepted--as of July 1, 1954.

Now, the first six weeks to two months she spent at Johns Hopkins with Manfred Mayer, an immunologist, learning all about the CF test. She came here in September of that year, and I gave her a laboratory. And the reason for bringing Nathalie here was I needed an alter ego--somebody to work with me on these things. So she was the first full time Virus Lab staff member aside from myself to come into the laboratory.

About that time [1954], Harald Johnson arrived on the scene, too. He came from India directly to my lab in Berkeley. He was with the Rockefeller Foundation, and after two tours of duty, as I recall, in India, he was assigned to the Virus Laboratory here. But he was entirely supported by the Rockefeller Foundation--salary and laboratory.

Nathalie was supported by funds from the National Foundation for Infantile Paralysis. Some years later we converted her soft money position into a permanent state position.

Her interest originally was in the enteric viruses--ECHO viruses, coxsackie viruses. Now, to put this in perspective: At that time, we didn't know very much about the enteric viruses. We knew that polio viruses were present, but then there was a whole phlethora of viruses which were turned up, which were called ECHO viruses. They were named pretty much after an observation such as Albert Sabin's, that these were Enteric Cytopathic Human Orphan viruses. Here we had cytopathic agents which we couldn't relate to a disease. So we got involved in the enteric virus field because

Lennette: the national foundation was setting up field trials in connection with the Salk vaccine. As I think we mentioned earlier, the Virus Laboratory at that time expanded into Acton Street, became the reference center for eleven western states.

And Nathalie went on from there. She worked on a lot of agents. She got involved in polio, coxsackie viruses, then went on to rubella. And we were part of the team that worked with other investigators with the Center for Disease Control to develop a uniform method for testing for rubella, because up to this point there were disparate techniques all getting different answers. A number of the investigators, for example Dorothy Horstman at Yale, Nathalie here, several people from CDC, like Kenneth Herrmann, and additional public health labs, all tested the same material by the methods they had handy in their own labs, and then CDC tried to put this all together. The results were incredibly bad. Everybody had a different approach: the answers didn't jibe. But out of that cooperative network came a standardized test which is still being used; that's the red cell agglutination inhibition test.

Hughes: Now, did CDC come up with that test eventually?

Lennette: Well, it was standardized by CDC, but everybody contributed basic data on the test. We had several meetings in which suggestions were made as to how the nonspecific agglutinins could be removed, leaving behind the specifics. And the problem today is that it is difficult to get hemagglutination antigens from rubella. No industrial houses want to produce them--not too big a market--or if they do produce them, they aren't very good. And this perhaps is where Virion might come in, because it is a European operator in the unusual position in that they manufacture these reagents, but they also use them in their own diagnostic laboratories, which cover much of virology for all of Switzerland. So it's obvious that they're making it, and they're also using it, but it isn't enough--it doesn't reach the American market. So I think that Virion could do a very valuable service.

But anyway, Nathalie worked on rubella and then she also got involved in varicella, both in the nature of the virus in man, and also she showed the connection with varicella virus of primates, working with people at the Delta Primate Research Center outside of New Orleans. She worked on hepatitis virus diagnosis--detection of the surface antigen.

Hughes: How did these different projects arise?

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Lennette: There are fads in medicine and science just as there are in other human relations. But above and beyond that, we were a diagnostic laboratory, and when the rubella virus was first cultivated by two different groups, Walter Reed Army Institute and people at Harvard, we learned what the techniques were and we began to apply them to diagnostic virology as practiced in a state health laboratory.

So we learned how to grow the rubella virus; we learned how to do the interference test, which was the hard way around, and eventually, as techniques developed, we went with them. You see, the mandate from the Rockefeller Foundation was to develop new diagnostic tests for viral diseases and to improve and simplify those which were already available. So we had to learn how to grow rubella virus; we had to learn how to do the hemagglutination test. Then, when cultivation of varicella virus was described, we got into the act, too.

We tried to learn from the literature how to grow varicella virus. Maybe Nathalie Schmidt and one of the technologists on the staff would do this. As soon as they got pretty good they would train another person so the whole staff eventually was trained. That's how we got into these new viruses, mostly because, as I say, each was a bandwagon. This is a new virus; everybody jumps on the bandwagon because here's a chance to find out new information. It's kind of exciting to work on a new agent.

Secondly, we're a diagnostic laboratory and we are very pragmatic. We want to do applied virology. The academic people aren't too concerned about that. They want to know all about how to grow the virus and how many turns there are in the DNA spiral and how many angstroms between them, and that kind of business, which to us is only secondary.

Hughes: We're talking about the fifties and the sixties?

Lennette: Yes.

#### Administration of the Virus Laboratory

Hughes: You were pretty busy with administration, were you not? How much were you in the lab in those years?

Lennette: Well, during the Q fever days I spent a lot of time in the fields wrestling sheep along with the rest of the crew. I spent a little time in the lab. Then when the field trials came along on poliomyelitis, as I mentioned earlier, I was trying to hold the front door closed. I didn't want to let these people in. But Malcolm Merrill and the chief of the health department, Halvorson, opened the back door and let the polio foundation people in, so here all of a sudden I was given this huge project, plus all the space and all the money required. So we just grew suddenly in one big spurt!

This was later added to by the development of a research program on cancer, of which virology was an integral part and a very important part. Here again we were given a project which we weren't especially anxious to have, but it was mandated to us. So the laboratory then got to be a good-sized lab. At its peak we had a hundred and fifty, a hundred and sixty people. Administratively it was almost a nightmare if you tried to work in the lab or in the field also. I ended up really working in the laboratory as an administrator and making pilgrimages to Washington about every three weeks. This went on for years. And yet that was the basis for the success of the laboratory because it was well supported.

Hughes: How did you maintain touch with investigators such as Nathalie Schmidt?

Lennette: I knew everything that was going on in the laboratory. Many people on the staff were surprised when I knew some of the things they were doing, and some things that were wrong.

Hughes: How did you know?

Lennette: Because I kept my ear to the ground and I talked to all of the staff whenever I had the opportunity--not so much through staff meetings, but to talk to them individually, to spend a little bit of time. You don't have to spend an hour or two. In just casual conversations of ten or fifteen minutes' duration you can pick up a lot of information if you focus your questions. I was also educated by that same process, you see.

Hughes: What happened at the staff meetings? Was that a more formal situation?

Lennette: We had a staff meeting every week. They were called to keep people advised of what was happening in Washington, in large part, because I was on the study sections for years. I was one of the first members of the study section on viral and bacterial diseases, so called, in 1949. During the second year of the section, I became co-chairman with John Paul from the department of preventive medicine at Yale. Just by attending those meetings you had some idea of what kind of research was being done in virology.

Lennette: Number two, you had an opportunity to meet a lot of these people at the National Institutes of Health. That was very helpful in finding out what federal funding sources have money and to which you might apply for support. That was my function as expediter and protector of the laboratory. We did have administrative problems with Sacramento, of course, and it was up to me to protect the staff so they could do their research and not be burdened with a lot of red tape and administrative detail. I took care of all that. For years I wrote the research grants. To do that I had to know a great deal about what was going on in the field and also in the laboratories.

Hughes: But the staff meetings per se were more external information as it applied to the Virus Lab rather than familiarizing the different groups within the Virus Laboratory with what each was doing.

Lennette: We did that by a monthly meeting (which still continues) in which an investigator on the staff would present a summary of the research that he was doing so that everybody knew what was going on in the laboratory and what progress was being made. These were informal, but slides were made and projected, and everybody had a chance to ask questions or make suggestions. Those were very good meetings; still are.

The laboratory was not run by committee. We had the staff meetings, and when we had a professional staff of ten or twelve or fourteen people sitting around a table they all had input. Questions were raised. We got their suggestions. Sometimes the consensus was to do something which I then might very well approve, or ignore and do something else instead, reminding everybody I appreciated their input and I liked to have the background, but on the other hand I was the responsible person. I'm talking about millions of dollars in the laboratory and a staff of a hundred and fifty people. If I felt that the consensus was not in accord with what should be done, I did it my own way.

Hughes: Was that usually accepted?

Lennette: Yes. They had little choice. I was pretty dictatorial about some of these things. There was no question either here in Berkeley or in Sacramento as to who ran the laboratory.

Nathalie Schmidt (continued)

Hughes: What else about Nathalie Schmidt?

Lennette: Well, she became an investigator in her own right. She worked on the coxsackie viruses and the polio viruses, hepatitis B, varicella, rubella, on the adenoviruses. She did a fair amount of work in immunology, also such things as rheumatoid factor and IgM [immunoglobulin M].

Hughes: Did she have a formal background in immunology?

Lennette: No, but she acquired all this as she went along. She read the literature widely. She was well versed. Basically she was a very bright person, outstanding in my estimate.

Hughes: You spoke of a memorial lecture.

Lennette: Yes. I'm trying to arrange this through Virion U.S. I've discussed this with the people in Clearwater, the University of South Florida, who sponsor a clinical virology meeting in Florida each year. I approached the organizers, Dr. Stephen Specter and Gerald Lancz, about setting up a memorial lecture, the Nathalie J. Schmidt Lecture, which would be given each year at Clearwater--this meeting brings in a lot of virologists from the eastern part of the country--either as a banquet presentation or as a keynote address, as the case may be. Virion would pay the travel expenses of the investigator or speaker, plus an honorarium, plus one or two days expenses at the meeting. This would be done each year.

I would expect also to organize something here on the West Coast, with meetings which are organized by Dr. Luis de la Maza at U.C. Irvine. That's a big West Coast virology meeting. I'm trying to get those two groups together to alternate every other year. Actually, I tried to do this alternation earlier. If you're having a meeting each year, first of all, you've got to compete with each other for speakers, and second, you can run out of talent in a hurry. So when you get down to the third, fourth, and fifth level of speakers, you're dead. Nobody wants to hear those people because you're going to get so many hacks. You want outstanding people who are making the science, not following. We want the movers and shakers, in a word.

Hughes: How widely known is Nathalie?

Lennette: She was widely known everywhere all over the world. She had quite a few students who came from various countries, various continents. As a matter of fact, at the time of her death she had two students here from mainland China. So she was very well known. She herself rarely went to a meeting, so that many people knew her by reputation rather than having met her.

Hughes: Why did she not go to meetings?

Lennette: She didn't think it was worthwhile in part, and secondly she was not the kind of person who wanted to mingle. She was in a sense reclusive. That isn't quite the word, no, she was more a "private person." She just didn't mingle too well in large groups. Which is not unusual. John Enders used to be the same way. He rarely went to a meeting anywhere.

#### Virion, Inc.

Hughes: You mentioned Virion in passing. Why don't you explain how you became associated with the company, and what your responsibilities are?

Lennette: Well, I got into Virion through a telephone call with an old friend, Joel Warren. Joel had been trained at Walter Reed Army Institute--at that time Walter Reed Hospital--under Joseph Smadel, who was one of the top virologists in the country. Joel also did graduate work under Albert Sabin in Cincinnati. Then he went on to several other positions, including some years at Pfizer. He left Pfizer and went to Nova University in south Florida, and then became director of the Goodwin Institute for Cancer Research at Plantation, Florida, near Fort Lauderdale.

Institute Virion Diagnostic Laboratories in Zurich which, as I mentioned, manufactures diagnostic antigens for bacteriology, parasitology, and virology, wanted to enter the U.S. market because they had been hearing about the need for these reagents, especially antigens for these various viral diseases. Because of the difficulty people were experiencing in this country in obtaining these antigens, they thought they could fill part of that niche.

Hughes: Why would Virion think that it could make a financial go, where the other companies obviously had made a decision that they couldn't?

Lennette: Well, the companies who were making these reagents were doing it on a small scale. They were selling it to laboratories. There were a number of firms, but the two major ones were Flow Laboratories and M.A. Bioproducts, at that time known as Microbiological

Lennette: Associates. They had the major portion of the market. Mind you, even so the major portion was small potatoes compared to say \$90,000,000 a year for Abbott producing hepatitis reagents. Virion had no plans to get into a \$90,000,000 market, but they felt that there was need for reagents, at least on a modest scale. Philosophically I had the same approach because I felt that nobody was taking care of the small laboratories.

I can diverge for a moment. At the meeting in Clearwater last year, in April of 1986, there was the Pan American Group for Rapid Viral Diagnosis. It was a co-sponsor or a host for this clinical virologists' symposium set up by the University of South Florida. The first morning was devoted to rapid diagnosis.

At the close of that session I got up and made the remark, "Gentlemen, you're talking to yourselves. You're not talking to the audience. You're talking about the way things are done at Children's Hospital in Boston, Children's Hospital in Philadelphia, Colorado Medical Center, U.C. San Francisco, where there are big budgets and ample staff, and you can do whatever you wish. But no small laboratory in a community hospital could do this kind of thing at the cost which is involved. Some of these tests are very labor intensive."

The audience was well-represented by lab techs. They appreciated what I was saying, because in a sense I was their representative, their spokesman. Actually, all the knowledge of virology and diagnosis doesn't reside within the medical schools; it's done in the small hospital. That's where we should do it, the first step in primary care.

So Virion was of the same mind, that these small laboratories were not being taken care of, and maybe they could get in there and compete with people like Flow or M.A. Bioproducts, or Orthodiagnosics, or Ciba, or some of the others, because they were producing antigens on which the comments were good, bad, or indifferent, the quality control was so variable. Some of that, there's reason to believe, was true, from experience.

Now how do you get into the American market? Whom do we know? [Virion asked.] They didn't know anybody, so they asked their bankers whom they could approach in the United States. One of the bankers there knew a former ex-banker, a young man who had been in the banking business and was earning a very good salary and decided this wasn't for him; he thought he would go to medical school. So he came to the States; he went to medical school; he was in the air force; he became an American citizen, and was practicing internal medicine at Fort Lauderdale. Through this banker in Zurich they got in touch with this internist at Fort Lauderdale and asked, "Whom do you know in virology that could help us?"

Lennette: He said, I don't know, but I will find out from the pathologist at our hospital. He posed the question to the hospital pathologist, William Russell. Russell said, "Well, you have a virologist right here in Plantation," -- which is next door to Fort Lauderdale -- "by the name of Joel Warren. Why don't you talk to him?"

So he called Joel Warren; told him what the problem was, and [asked] could he help. Joel said, "Sure, I think I could help out." Whereupon he called me, knowing that I had been in a diagnostic virology lab, was still there, and [asked] would I care to be a partner with him in this.

It turns out I knew Bill Russell from way back, because he used to be the pathologist for Cottage Hospital down in Santa Barbara. I also knew him when he was in St. Louis. It's a small world. Warren arranged to meet with the president of Institute Virion. This was at the ASM [American Society of Microbiology] meeting in St. Louis in 1983. So Joel flew up from Fort Lauderdale. I came in from Berkeley. I was going to go to St. Louis anyway, to the meetings, because my older son lives in St. Louis, so I was going to see the grandchildren and also go to the meetings there, and meet with this man whom I'd never met by the name of Viktor Gassler, who's the president of Virion.

However, one afternoon I wandered into the exhibit hall and I saw this purple sign way down at the end of a dimly lit exhibition corridor, "Virion." I had never heard of Virion except incidentally. I went down to see what their products were. This was all being explained to me by a young man on the Virion staff, a South American. Just about that time, in comes this older gentleman, who was Dr. Gassler, but I didn't know that at the moment. I asked him what the products were, and what they were making, and what the costs might be.

I said, "Well, I would like to have a list of all this."

He said, "Give me your name and your address and phone number." I gave him my card. He looked at the card, then recognized the name. He said, "Just the person we want to talk to." So the three of us, he, Warren, and I, had dinner that night.

As it turned out, Warren bowed out of the picture and that left only me. He had already been to Zurich--he had spent a week there--and then they invited me to come over and spend a week and discuss matters with them. I said, "Well, I'm not doing anything. Sure, I've got free time. I'll give you a hand with this."

Lennette: We made an agreement that I would help them to write the package inserts which are necessary for FDA [Federal Drug Administration] clearances. We spent a lot of time doing that. I spent over a year. Then as things developed, they decided they would form a U.S. subsidiary called Virion U.S., Incorporated. They had it all chartered in Delaware as a Delaware company. All they had to do was activate it. In January of 1985 they decided to have a meeting in New York to try to get some possible sales people here, and also in Canada, and could I set up the meetings with various people whom they had in mind, which I did. Another meeting was to be held in New York with the attorneys representing Virion.

We met with some of these marketing people. It was an eye-opening experience for me how they went about all of this. Then there was to be one morning that we spent with the attorneys on Park Avenue--it was a big law firm--which we did. It was arranged with myself and Viktor Gassler, the president of Virion, and Hans Bucher, vice-president of Virion, and also an influential and affluent backer of Virion on one side of the table, and the U.S. attorneys on the other side. Peter Scheiss, who was the Virion business representative in Morristown, New Jersey--he represented a number of foreign firms, and is an accountant--also represented Virion. He was there, too.

The papers came across the table from the attorneys, and here it was. Lennette was to be the president of this organization, which was news to him. Gassler was going to be vice-president, and Bucher would be the secretary-treasurer. Peter, I forgot what he would be. Anyway, there were four of us.

So this corporation was born at midday--I forgot the exact date--January 1985. It's been expanding. I spent a lot of time in Zurich going over there for intervals of a month at a time. Last February [1986] I was there the end of January and all of February, five weeks. I was there all of July, and I'm going back for another five weeks at the end of November.

Hughes: Now that you've written package inserts...

Lennette: No, we haven't. We're still working on that because it's a very slow and time-consuming process to move anything through the Food and Drug Administration. But Virion is delighted because they have somebody in this country who knows people in the FDA, can work with them--not pounding on the table and asserting his clout but working with these people--and making them one of the few European companies that could get FDA approval. Virion left the competition behind. So they're very appreciative of that.

Lennette: What came out of all this work was we have prepared a standard description for the complement fixation test. That's boilerplate now. All they have to do is organize it and put it into each package insert. The things that will be different will be the epidemiology and the clinical picture, this sort of thing. A list of reagents. The equipment is pretty much the same. With just minor changes in the text you have a package insert. We have about thirty of these to do, plus the fact we want to write a couple of monographs on some of the problems of diagnostic virology, rheumatoid factor, IgM, to bring together all of this very diverse literature into a package so it can be evaluated. We have an immunologist now doing this at Lausanne University. So we're going to produce the monographs, but we're looking for some help to get these package inserts finished.

I spend so much time in Zurich that Virion is talking about buying an apartment that I could use over there. Not entirely for me, because they have visitors who could use it too, but when I'm there I get first crack at it. I already have a company car whenever I'm there so I can get around. With an apartment and a car I'll have considerable reason to stay there and get things done without hurrying back.

Hughes: Are you able to call upon your friends in the FDA specifically?

Lennette: No. I don't have any what you would call friends. I work with two women and one man on these package inserts. The woman in bacteriology is easy to work with and I work fine with her.

Hughes: Is this long distance?

Lennette: All by telephone. The Virion people were dumbfounded when I said I had spent something like fourteen or fifteen months entirely by telephone, that I had never seen these people. They just couldn't understand how you could do this. I said, "Well, you can do it in this country."

But the one that was doing the virology part was new to the field. Her background was hematology. So she asked a lot of questions and we had a lot of nitpicking to go through. She didn't know who I was.

Hughes: They're looking at it just from the scientific standpoint. Is anybody looking at it from the standpoint of competition?

Lennette: No.

Hughes: That doesn't bother them?

Lennette: No. The FDA wants three things. They want this to be scientifically correct. Number two, it must be lucid and clear to the technicians who are going to use those directions. And number three, to protect the producer, don't make statements that open him to libel or liability.

Hughes: Is it a concern of the FDA when a foreign company comes in and wants to market in the States?

Lennette: No different, but you've got to have somebody here that can take up the cudgels for you. Otherwise you do it by mail.

Here's an example. We sent in a package insert to the FDA. If it's sent from Zurich, it takes seven to ten days to reach Washington. The FDA goes over it and they send you back some ideas and suggestions of what ought to be done. That takes seven to ten days to get back to Zurich. Now you have thirty days in which to respond, of which about anywhere from fifteen to twenty are gone by mail. That doesn't give you much time for people who work in Zurich to get it back to me for my approval and forward it. So what do we do? We just set up a facsimile machine in my home and in the Virion office. So anything that comes to me from the FDA gets here in three or four days. I immediately fax it to Zurich, let them get working on it, and I work on it, too. As soon as they get their end done, they fax it to me. I put it together, fax it back there, their office staff types it, and we send it off by Federal Express to the FDA. It's the rapidity with which we work.

This is sort of beyond what the Europeans would do. There're very few Europeans who even want to get involved to get through FDA for the diagnostic reagents. They don't think it's worth their time because they don't think that they're ever going to get it approved. Well, if they have good products they get them approved, but FDA insists that you give them the basic data that shows that your results are equivalent to the results obtained by other methods, by other laboratories. So I have to set that up for Virion, too; call in people to do the testing using Virion reagents and their own reagents and see how the answers on these specimens come out. If you have too much variation, of course, you don't get approval. This has taken a lot of time. They were amazed that so much of this was accomplished in so short a time.

Hughes: Is your tenure there finite? Once the products are approved by the FDA, then you drop out of the picture as far as Virion is concerned?

Lennette: No. They want to have a subsidiary here, and want me to run it. What they will do is have a business office here, maybe Peter coming in full time, and I would be here as the president of Virion U.S., and perhaps eventually set up a production facility, because all their reagents are being produced in Zurich. As these new tests come along, like ELISA [Enzyme Linked ImmunoSorbent Assay] or latex agglutination or whatever, these people have to get into that market. You have a situation with Dr. Mirko Jung that really is unusual. He makes all these reagents, but one person can do only so much. If they're going to expand, he's going to have to have an alter ego that he can trust, or else turn it over to Virion U.S., which means building a production facility or finding laboratory space, which would be my job. I got into this only because it was a challenge to get these things together and try to market them and get them to the smaller laboratories, and make some of these things which are essentially orphan reagents. They're going to have a huge market. You're supplying a real need.

Hughes: Will you be involved, at least peripherally, with the marketing as well?

Lennette: Well, Dr. Jung doesn't want me to get involved in the marketing. He thinks of me as a scientist and I ought to stick with science and work with him on some of these things. I agree.

Hughes: I was thinking, though, that you might be aware of the American laboratories that might be interested in such products.

Lennette: Yes. But on the other hand, Dr. Gassler thinks I ought to be involved in the marketing. He thinks I'm the logical person to do it. The extent to which I've gotten involved is to open a few doors for Peter and Gassler to enter. When Gassler was here, he talked to a number of people across the country, made the initial contacts, and Peter has followed up. But Peter follows up only by shipping the reagents that are requested by somebody. There's never a phone call to follow up, "What's happened? Why don't you order from us again? Is the stuff so poor?"

I have run into a marketing person who's looking for a challenging position. He doesn't want to get involved in a firm which already has an established marketing group so that he walks in and inherits the deadwood and mistakes of a line of his predecessors.

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Channing Cornell is the marketer I have selected, and who wants to start small and to use the telemarket approach. Get a young person in to sit by a telephone and just call up all these clients who had ordered something and ask them how good it was, or what was their experience, could it be improved, and this sort of thing. But

Lenette: keep following up to see whether these people are purchasing or if they aren't, and also contact possible new clients. That isn't difficult because we have the mailing lists that we get from the ASM and just sort of weed out the people who are in food bacteriology or dairy bacteriology or water bacteriology or whatever. They'd just pick people in the medical field. So we have quite a list of about three thousand people and we're going to follow up on those. We've also been advertising in the Journal of Clinical Microbiology. For this year the ads will appear in January, February, and March [1987], about half a page or a whole page. We will have an 800 number in there, and if we can work it out, the booth number at the annual ASM meeting where they can visit people. Peter will be there, and Viktor Gassler will be there, and also Cornell who's going to do the marketing, if they accept him. He's having a meeting with them next month, November 17th, in New York, and probably with Dr. Josephine Mosiman from the diagnostic unit of Virion in Zurich. They will spend that whole week at the ASM meeting, which is scheduled for Atlanta in March.

So things are moving. Now is a propitious moment because Flow, which got into a real argument with Food and Drug, finally closed down--not because they were culpable but because of orders from FDA to do something that was ridiculous. That was that these reagents that Flow was producing should be pyrogen-free! Now why in God's name something which you're using in a test tube has to be pyrogen-free is beyond all of us. On that basis Flow was closed down for some weeks, several months, so they finally said, "Well, we don't need this. We've had enough hassles with FDA. Life is too short. To hell with it."

So they have sold all of their inventory of cell cultures and reagents to a small laboratory here in Marin called Earl Clay. Earl Clay wants to keep all the cell lines and all of the cells that they have. They don't want the diagnostic reagents. They're trying to sell those to somebody else. If they give Virion a good price, we'll buy them, but it has to be a good price. Otherwise we can make them ourselves. Earl Clay is now beginning to get large and people are beginning to complain about them, that you can't get the service that you got a year or two ago. They gave good service, but are paying the price of fast growth.

The upshot is, you can't depend on one or two suppliers. You ought to have three, four, or five if you can. If one has problems and he's your sole source, you're dead. So they're anxious to have a second supplier. Maybe Virion can do that.

Hughes: So you think that people in this country will welcome Virion?

Lennette: Oh, sure, but they've got to have quality reagents, too. Secondly, they're very cognizant of what is a real problem. Mainly, that's availability. Some of these people make X milliliters of a reagent and that's it. You make an order; two days later they're out. They back order your purchase for three months. They make up a new batch, let's say, five hundred milliliters. That's no way to do things. They do that, I think in part, because the shelf life of their reagents is so short. They don't want to make up liters and liters and have to throw them away. On the other hand, it's the way they package the material that gives it such a short shelf life, because they put it into vials from which the material may be lyophilized. The tube has rubber stoppers in it, and with time the stoppers leak. Then you get rehydration, which is very, very subtle, but it destroys your antigen.

Virion avoids this by dessication-lyophilization in glass ampoules. The ampoules are in a vacuum during drying, and at the end in an inert gas. Argon is used because it is heavier than air, so it stays in the ampoules when you bring them out into the ambient atmosphere of the laboratory--and then they're flame-sealed. So you get lyophilized material in glass vials with an inert gas, and they're flame-sealed. The contents keep forever.

FDA questioned me, "What do you mean, 'It will keep indefinitely'? What are your data? What's your evidence?" I pointed out there was some very good evidence published in 1949 by Earl Flossdorf from the University of Pennsylvania. This is a whole new generation who doesn't know what's transpired in the past. They have no knowledge of how to do things or what literature there exists.

I settled that argument by sending a copy of a letter which I received from the University of Otago in New Zealand. One of their virologists there had opened an ampoule of the Spirup strain of influenza A virus and wanted to know the history of this virus. Had it come from man or from birds or from animals? We had records here. He knew it came from our lab. He said, "Furthermore, you might be interested to know that I rehydrated some of this material, put it in tissue culture and in embryonated eggs and it just grew right out."

This was lyophilized in 1949, and this lab was testing it in 1986. Thirty-seven years. I just made a copy of his letter, sent it to the FDA. No comment. That settled the issue.

Hughes: Well, Dr. Lennette, is there anything at all that you think of adding?

Lennette: I would have to go through and read the transcript. I can't think of anything.

Satisfactions and Contributions

Hughes: I have two questions in conclusion. First of all, what period or periods of your career did you enjoy the most?

Lennette: Right here in Berkeley.

Hughes: What stage?

Lennette: I think all of it, except towards the end, the cancer field. I wasn't all that wrapped up in the cancer field. But it had to be done. It was fun working with Bob Huebner and Murray Gardner, who is now at Davis. Gardner was a pathologist at USC [University of Southern California] Medical School working on tumor viruses. Gardner got the Davis group and our Virus Lab working together on AIDS. A very competent person. It was fun working with these people. I've enjoyed my whole career here. I've had a wonderful time. I've enjoyed all of it. I think that life is too short to be working in a job that you don't like.

After I dropped out of the University of Chicago in 1927 I worked in New York for two years to improve my finances to go back to the university. I worked in the accounting department of a large chemical company, and I disliked every day of those two years. Apparently I did all right, because when I was leaving the people really wanted me to stay on because they saw a future for me. I said, "I don't have any future here." It was a cost accounting department; I don't like cost accounting, so I left. It was traumatic but necessary.

I enjoyed my stay here. I thought it was fun.

Hughes: Was it the people primarily?

Lennette: The people in the laboratory I worked with, plus the fact that I had support within the department. I had complete freedom to do whatever I wished. There were no inhibitions on anything I wanted to do, and in the early days I had the support from Sacramento, in the days when Earl Warren was the governor. He was very health-minded, and he helped to develop the Virus Laboratory because he gave us so much money. Then after he left office, Pat Brown came in, and Pat too was very supportive. After that we just had a series of so-so governors, like Goodie Knight, who didn't pay much attention to what was going on. He was sort of a passive governor. Then we worked up to Reagan, who was kind of a disaster because he wanted his finger in everything that was going on. Then we had Jerry Brown, who was so flaky. Things aren't what they used to be in the older days when we had all that support. But I had a good time. I enjoyed it. There are some projects I think I would have chosen over the ones I actually worked on. It would have been much more productive and more interesting.

Hughes: But you didn't always have that choice when it was mandated?

Lennette: No.

Hughes: What do you consider to be your greatest contribution?

Lennette: Well, from the standpoint of interest, I think it was Q fever.

Hughes: Interest? Do you mean to other microbiologists?

Lennette: To me. Q fever is not a viral disease but due to a rickettsia, which happens to be a bacterium, as we learned later on. But that was interesting to me because I was in the field and I got my hands dirty, messing around with those dirty sheep, especially at lambing time. It was raining out there on the range; it was bitter cold. Nothing would stop that howling wind coming down from the arctic regions. Lambs being dropped all over the landscape. It was hard, difficult work, but it was enjoyable. In the lab things were interesting because we were learning so many things.

The other interesting area was the development of some of these diagnostic procedures, such as for rubella, which was more Nathalie Schmidt's field than mine. But we served a real function by making believers out of certain academic people and by being pragmatic. A test or procedure might be fine for somebody in the University of California Medical School, but it certainly wasn't applicable to a health department or a small clinical laboratory. Our problems are different. And then mind you, the Virus Laboratory was in the state health department. It was not a virus laboratory for the clinician, because the diagnoses were too far after the illness to be useful. It was epidemiologically-oriented, so we learned a lot of epidemiology in those years.

Today now, with antivirals on the scene and all the emphasis on rapid viral diagnosis, that's the way to go. But as usual, the pendulum has gone too far in one direction, and I now try to keep these people on an even keel, get up as I did at Clearwater and tell them the facts of life.

You want direct detection of a virus in the throat or in the nasopharynx. So you make a swab, or you curette and you get some cells, depending where the lesion is, and you apply a direct technique, either immunofluorescence or an ELISA method, and you find the antigen. I would point out some of these viruses may be adventitious. We know very little, compared to the bacteriologists, of what the normal viral flora of the nasopharynx, the respiratory tract, is. So you have to know what these viruses are doing in the first place, and which of them are pathogenic and are causing the disease. It isn't easy.

Lennette: In any case, I've mentioned diagnosis and this brings up one other aspect. September 30, 1986, I was given the Pan American Groups for Rapid Viral Diagnosis Wellcome Award in Rapid Viral Diagnosis in recognition for establishing and teaching viral diagnosis.\*

Hughes: Is that a good note to end on?

Lennette: I guess so.

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\*See appendix for a copy of Stanley A. Plotkin's speech on the occasion of the presentation of this award to Dr. Lennette.

V ADDENDUM II: JULY 21, 1987  
 Written by Dr. Lennette

Family Background and Education

- Hughes: In our first interview, we discussed your family background. In reviewing this material recently, it seemed to me the coverage was perhaps incomplete, and I thought you might like to add to it.
- Lennette: I think you are quite correct, and believe we might add several points in order to round out the picture.

My parents came to this country at a very early age with my grandparents so that they grew up in an ambiance that culturally and linguistically made them Americans although they understood and valued the culture and traditions of their European heritage. In keeping with the Victorian values and philosophy of the times, my parents married at an early age; at the time of their marriage in late 1906, my mother was eighteen years of age, my father twenty. Both my maternal and paternal grandparents were residents of Pittsburgh, Pennsylvania, specifically an area known as Belzhoover, at that time at the end of the streetcar line, so virtually in the open country or a suburb. I was born in Pittsburgh in 1908, my sister, Henrietta, in 1910.

My earliest recollection in my childhood is living in what is termed an "extended family"; at various times, several aunts and uncles with their children lived in this four-story house which stands out in my early remembrances. My paternal grandfather, the patriarch of the family, was a real autocrat and a real disciplinarian--everybody had to "shape up," including all the grandchildren irrespective of age.

I have very few recollections of my father. Their marriage did not work out and terminated in a divorce when I was, insofar as I can gather, about five or six years of age. My mother, my sister, and I moved to the second-floor apartment of a two-flat

Lennette: house on the south side of Pittsburgh, where I received my grade school education at the Humboldt School and my secondary education at South High School.

These were difficult times for my mother, attempting to bring up two children with no assistance from my father, and too proud to accept help from his parents. My mother found employment as the head of a culinary department in one of the medium-sized Pittsburgh hotels, and not only arranged the menus, purchased the requisite supplies, but also not infrequently served as a chef. Her hours were long and demanding so she saw little of her children except in the late evenings and at night. During the day, we attended school and solicitous neighbors looked after our well-being. My mother's greatest wish was that both her children have a good education, and in my case especially, she inculcated a desire for a college and a professional education, this in an era where a high school education was the end of the educational process, and a college degree essentially a rarity.

My mother was a hard-working, affectionate, and loving person, and we children reciprocated that love. Indeed, whatever I have accomplished during my lifetime, and especially during my professional career, I owe in large part to her support and understanding and deep desire to see me enter a profession, and especially medicine, in which I had earlier professed a deep interest. Unfortunately, she never lived to see me attain this objective because she died of cancer in 1926 at the age of thirty-eight and at a time when I had only completed my high school education and was ready to enter the university.

Upon the death of my mother, our small family was broken up. I went to Chicago to live with an aunt and entered the University of Chicago. My sister went to live with my grandfather's former housekeeper with whom she lived until she finished her high school education, was eligible for employment, and shortly thereafter married into a relatively affluent north side Pittsburgh family.

Hughes: Can you tell us about your wife, Elizabeth?

Lennette: My wife's family resided in St. Clairboro, a south hills suburb of Pittsburgh. Since very few of these small outlying areas were able to support school systems of their own, Elizabeth attended Langley High School, near McKeesrocks, on the west side of Pittsburgh. I met her through Virginia Coates, a classmate who also resided in St. Clairboro, but attended South High School.

To most young people of that time, New York City was the mecca towards which those interested in the arts, literature, the theater, and business were attracted and migrated. After graduation from

Lennette: high school, Elizabeth spent two years at Frick Teachers' Training College and acquired a teaching certificate. However, a teaching career did not appeal to her, hence she went to New York City and found employment with a high-ranking manufacturer (Wear-Right Company) and distributor of women's dress gloves. Actually, she worked as an administrative assistant and secretary, but also served as a model for gloves because she had such beautiful hands (the ads always showed one hand gloved, and the other ungloved).

After one year at the University of Chicago (1926-27), I too went to New York to find employment and save up money for my return to the university as well as to be near Elizabeth.

I returned to Chicago in the fall of 1929, just ahead of the collapse of the Wall Street market and the beginning of the Great Depression, and Elizabeth came several months later. She found employment with the General Motors Corporation while I attended the University of Chicago, and we were married in September 1930 at the beginning of my senior year in the University of Chicago.

As was brought out earlier, I did all of my graduate work towards the degree of doctor of philosophy in microbiology at the University of Chicago and also all of my medical training at Rush Medical College at the University of Chicago. I obtained my Ph.D. in 1935, my M.D. in 1936, and all of this I owe to Elizabeth who made it possible. It was a marriage based on love and affection and mutual respect and, something unusual in these days, it was a permanent union, one that endured for fifty-one years until Elizabeth's death in 1981.

#### Paul and David Lennette

Lennette: Up to the time of the Second World War, that is, during the 1930s and 1940s, scholarships and fellowships existed, but were very few in number. A large proportion of students in college and graduate schools had to earn their way on their own, and as a result marriages and families were postponed until after completion of one's studies. Elizabeth and I were in our "advanced years" when our family was founded. My oldest son, Edwin Paul, was born in June 1939, and the younger son, David Alan, was born in May 1945. Both attended local Berkeley and Oakland schools, and graduated from the University of California, Berkeley, Paul in chemistry and mathematics, and David in physics and mathematics. During the Vietnam conflict, Paul was inducted into the army, entering as a PFC at Fort Ord and emerging from his training period as a second lieutenant assigned to Edgewood Arsenal in Maryland. He served at Fort Sam Houston, in Nha Trang,

Lennette: Vietnam, and in Germany at the base hospital at Landstuhl. After six years service in the military he returned to the United States and took up his graduate studies in clinical chemistry at the University of Iowa, Iowa City. He is now the clinical chemist in the department of pathology, Belleville Memorial Hospital, Belleville, Illinois, and lives across the Mississippi River in Crestwood, Missouri. He married Jacquelyn Gross, an army nurse, and they have three children, Michael, Andrew, and Marie.

After graduation from the University of California, David married a classmate, Evelyne Tam, and both enrolled in the graduate school of Washington University, St. Louis, to work toward a doctoral degree in microbiology. Both received their Ph.D. degrees and moved to Philadelphia where David was on the faculty of Hahnemann Medical School and in charge of a newly established viral diagnostic laboratory in the department of microbiology. Evelyne in the meantime obtained an appointment in the Children's Hospital of Philadelphia to work with Werner and Gertrude Henle, pioneers in the development of knowledge on the Epstein-Barr virus.

Evelyne and David were in Philadelphia for several years, and then returned to Berkeley and opened their own private viral diagnostic laboratory in Emeryville, and several years ago moved the laboratory to Berkeley. They have a technical staff of a half dozen or so people but still find time to do research with some of their collaborators at the University of California, San Francisco, for example, Dr. Jay Levy, currently working on AIDS and its causal virus, as well as several faculty members in the School of Dentistry. They also work with other collaborators, including one working on leukemia in New York City. This, in large part, is a reflection of the respect with which medical investigators and scientists hold Virolab, Incorporated, which David and Evelyne founded.

#### More on the Virus Laboratory

Hughes: You described your assignment to the Rockefeller Foundation Laboratories at the California Department of Health in 1944. In 1946 you went to Camp Detrick and then returned to Berkeley in November 1947. Could you tell us something about the organization and functions of the Virus Laboratory when you took over as director?

Lennette: The first and foremost thing that I did was to notify the scientific community, particularly microbiologists and especially virologists, that the Viral and Rickettsial Disease Laboratory was devoted first to laboratory diagnosis of viral and rickettsial diseases, secondly



*Top Left:* Elizabeth and Paul Lennette, ca. 1944

*Bottom Left:* David, Edwin H., and Elizabeth Lennette

*Bottom Right:* Inta Ziedin, Edwin H. Lennette, Nathalie Schmidt, and Shirley Hagens on the patio of the Acton Street laboratory. Berkeley, Early 1950s.







David, Elizabeth, and Edwin H. Lennette at home in  
Oakland, California, 1963



The Lennettes with his sister, Henrietta Ede. 1963



Lennette: to research, and thirdly to training. That it would assist in the operations and investigations of the Bureau of Infectious Diseases of the health department was always taken for granted.

From the operational standpoint, the laboratory functioned well because of the structure which Dr. Eaton had established. It now remained to change the direction from an entirely pure research-oriented operation into one concerned with development of diagnostic methods and the provision of diagnostic services to the medical community. I was fortunate to have inherited Mrs. Alwine van Allen as the laboratory manager and, since the staff was very small, she could not only discharge her responsibilities as manager but also participate in work at the bench. Within a matter of a couple of years, however, the laboratory staff began to expand, in part because it quickly developed an international reputation as a diagnostic laboratory, and students and scientists were applying from all over the world. For example, in 1950 we had one physician from Norway, a veterinarian from Brazil, another from CDC, and a Mexican physician working for a doctoral degree in the School of Public Health at the University of California here at Berkeley.

Over the thirty-one years that I was director of the laboratory (1947-1978), dozens of scientists from all over the world participated in our training programs, and a number of students working for their doctoral degree at the University of California, Berkeley, did their doctoral thesis work in our laboratories. This is aside from the many technologists who were sent to Berkeley by various institutions and governments to learn something about diagnostic virology.

Having so many students eventually necessitated having at least one person whose major, or even sole, effort would be in the training area. In the early days this fell to Mrs. van Allen and various members of the staff assigned on occasion to assist her. However, with her retirement in 1966 I appointed Ms. Mary Martins as Training Officer. We did everything possible to make our visiting scientist fellows and students welcome. Mary met many of these people at the San Francisco airport and brought them to Berkeley where she had arranged accommodations for them. In the case of those visitors who brought their families with them, Mary made arrangements for apartments or even small houses. She saw that people were housed and comfortable, and acquainted them with the cultural events of the Bay Area. All in all she did a remarkable job, all this in addition to her activities with the Association of California Public Health Laboratory Directors. She helped to organize the early meetings, and over the years acted as the hostess at each meeting, personally arranging and taking care of all the social events.

Lennette: I managed to put together an excellent technical staff, many of whom participated in our research efforts, and some of whom went on to bigger, better, and more interesting things. Florence Jensen was in charge of our serology unit for many years; Helen Ho was in charge of the virus isolation unit; Tak Shinomoto was in charge of the virus identification section, etc. Jean Harris and Beatrice England worked as a pair in serology and in animal inoculation, but this team eventually broke up with Jean going on to become a full-time homemaker, and Bea took an appointment with the Sixth Army Area Medical Laboratory at Fort Baker in order to establish a viral diagnostic laboratory.

Inta Ziedins was seconded to St. Gallen, Switzerland to help establish a viral diagnostic unit at the institute. Beverly Jean Neff went on to the University of Michigan to earn a doctor of public health degree under Dr. Thomas Francis, Jr., professor of epidemiology in this school, and chairman of the Commission on Influenza of the Armed Forces Epidemiological Board. Similar careers awaited others on the staff. For example, Barbara Thompson left the laboratory to earn a doctoral degree in epidemiology at the UC School of Public Health across the street, and since then has worked in several positions dealing with epidemiologic studies.

Marjorie Maggs (who later married Francis Abinanti, our veterinarian in the Q fever project), together with Beverly Jean Neff, headed up the animal work in our Q fever studies. Frances Fujimoto, who was a registered nurse in addition to being a licensed public health microbiologist, worked for a time at Fort Ord on our influenza vaccine studies, and later was engaged in the studies on St. Louis and western equine encephalitis. Margaret Ota was a participant in these studies also, together with Koichi Nakamura.

The laboratory was among the very first to utilize fluorescent antibody methods, and pioneered the use of this technique for the diagnosis of rabies in animals. Jim Woodie, who assisted in much of this early fluorescent antibody work, eventually became the laboratory's expert on fluorescent antibody methods, which we applied to other areas of diagnostic virology. Anna Wiener was sent to the laboratory of Dr. John Enders to learn tissue culture methods in 1950, and helped to introduce the new tissue culture techniques into the Berkeley laboratory. This section was subsequently expanded with the appointment of Shirley Hagens and Virginia (Ginger) Fox to establish a tissue culture unit.

On the personal side, Carol Shon was my technologist and co-worker on a number of projects during my early days in Berkeley, and later took charge of the antigen and the serum preparation unit. Sachiko (Sachi) Yamamoto was my long-time secretary and administrative

Lennette: assistant and, after a hiatus of some years to bring up her family, returned to assist me on a part-time basis in the work of the California Public Health Foundation, of which, as you know, I serve as president and chairman of the board.

As you may gather from what I have just said, I take great pride in the competence and the abilities of my staff and in their expertise, and I am indebted to all of them for making the Viral and Rickettsial Disease Laboratory known and respected all over the world.

Transcribers: Sam J. Middlebrooks and David Pollack  
Final Typists: Shannon Page and Laurie Dunlap



## TAPE GUIDE--Edwin H. Lennette

Interview 1: August 13, 1982	1
tape 1, side A	1
tape 1, side B	11
tape 2, side A	22
tape 2, side B	33
Interview 2: September 23, 1982	
tape 3, side A	35
tape 3, side B	45
tape 4, side A	56
tape 4, side B	61
Interview 3: October 7, 1982	
tape 5, side A	74
tape 5, side B	86
tape 6, side A	98
tape 6, side B	blank
Interview 4: November 4, 1982	
tape 7, side A	110
tape 7, side B	114
tape 8, side A	125
tape 8, side B	136
Interview 5: November 15, 1982	
tape 9, side A	141
tape 9, side B	152
tape 10, side A	163
tape 10, side B	174
Interview 6: February 19, 1983	
tape 11, side A	175
tape 11, side B	186
tape 12, side A	197
tape 12, side B	204
Interview 7: February 3, 1983	
tape 13, side A	209
tape 13, side B	220

Interview 7: February 3, 1983	
tape 14, side A	229
tape 14, side B	blank
Interview 8: February 24, 1983	
tape 15, side A	239
tape 15, side B	249
tape 16, side A	259
tape 16, side B	269
tape 17, side A	279
tape 17, side B	blank
Interview 9: November 13, 1986	
tape 18, side A	288
tape 18, side B	296
tape 19, side A	307
tape 19, side B	blank

APPENDICES

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320  
APPENDIX A  
Curriculum Vitae

EDWIN H. LENNETTE

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Oakland, California 94611  
(415) 531-0461

State of California  
Department of Health Services  
2151 Berkeley Way  
Berkeley, California 94704  
(415) 540-2557

BIRTHDATE

September 11, 1908; Pittsburgh, Pennsylvania

EDUCATION

1931 B.S. University of Chicago  
1935 Ph.D. (Hygiene and Bacteriology) University of Chicago  
1936 M.D. Rush Medical College, University of Chicago

INTERNSHIP

1937- St. Luke's Hospital, Chicago  
1938

MEDICAL  
LICENSES

1938 Licensed to practice medicine in Illinois  
1946 Licensed to practice medicine in California

EXPERIENCE

1936- Instructor in Bacteriology, University of Chicago  
1937  
1937- Research Associate, University of Chicago  
1938  
1938- Instructor in Pathology, Washington University School of  
1939 Medicine, St. Louis  
1939- Staff Member, International Health Division of the Rockefeller  
1946 Foundation. Assigned to influenza studies at the Rockefeller  
Institute for Medical Research, 1939-1941; yellow fever studies  
in Brazil, 1941-1944; general virus research in the Rockefeller  
Foundation Laboratories at the California State Department of  
Public Health, Berkeley, 1944-1946  
1946- Chief, Medical-Veterinary Division, Camp Detrick, Maryland  
1947  
1947- Chief, Viral and Rickettsial Disease Laboratory, California  
1978 Department of Health  
1967- Chief of the Cancer Research Program, California Department  
1973 of Health  
1972- Chief, Laboratory Program, California State Department of  
1973 Public Health  
1973- Chief, Biomedical Laboratories, California Department of Health  
1978  
1978- Consultant, California Department of Health Services  
1981 Interim Director, W. Alton Jones Cell Science Center, Lake Placid  
N.Y.  
(Effective July 1, 1978, the former California Department  
of Health was reorganized and re-named the California  
Department of Health Services.)

PRESENT TEACHING APPOINTMENTS	1947-78	Lecturer in Virology and Epidemiology, School of Public Health University of California at Berkeley
CONSULTING PHYSICIAN	1948-80	Highland-General Hospital, Oakland, California
	1957--	Peralta Hospital, Oakland, California
DIPLOMATE	1950	American Board of Preventive Medicine and Public Health
	1961	American Board of Medical Microbiology
PUBLICATIONS		Author of more than 350 scientific publications. Complete list available on request.
HONORS	1934	Sigma Xi
	1949	Delta Omega, Zeta Chapter (President 1964-1965)
	1961	American Association of Immunologists (President 1966-1967)
	1967	Federation of American Societies for Experimental Biology (President 1968-1969)
	1968	Recognition Plaque for Work on Rubella from House of Delegates, California Medical Association
	1968	Gudekunst Memorial Lecture, School of Public Health, University of Michigan, Ann Arbor
	1969	Bronfman Award and Prize for Achievement in Public Health, APHA
	1970	I. M. Lewis Memorial Lecture, University of Texas, Dallas
	1970-71	American Epidemiological Society (Vice President 1970-1971)
	1970-74	Rush Medical College, Chicago Member, Board of Directors, Alumni Association
	1970-74	Tissue Culture Association, Inc. Member, Board of Trustees
	1971-74	Rush-Presbyterian-St. Luke's Medical Center, Chicago Member, Board of Trustees
	1972	Honorary Fellow, American Society of Clinical Pathologists
	1973	University of Oklahoma College of Health Distinguished Lecturer
	1973	Outstanding Civilian Service Medal, Department of the Army

HONORS  
(Continued)

- 1973-76 President, Armed Forces Epidemiological Board, Office of The Surgeon General, Department of the Army
- 1976-78 President, Tissue Culture Association, Inc.  
(First Vice President 1973-1975)  
(Past President 1978-1980)
- 1976 Wyeth Award in Clinical Microbiology and Prize, American Society for Microbiology
- 1978 President, American Society for Microbiology  
(Vice President 1977)
- 1980 Invitational Elizabeth Tambllyn Memorial Lecture, California State University, Los Angeles
- 1981 Professional Achievement Award, University of Chicago Alumni Association
- 1986 Burroughs-Wellcome Award for Rapid Viral Diagnosis
- 1986 Distinguished Alumnus Award, Rush Medical College, Chicago

## EDWIN H. LENNETTE

PRESENT  
APPOINTMENTS

- DEPARTMENT OF DEFENSE, DEPARTMENT OF THE ARMY
- 1948-- Consultant to Sixth Army Medical Laboratory
- NATIONAL ACADEMY OF SCIENCES--NATIONAL RESEARCH COUNCIL
- 1978-- Member, Safe Drinking Water Committee
- 1978-- Member, Subcommittee on the Efficacy of Disinfection,  
Safe Drinking Water Committee
- 1978-- Member, Committee on the Effects of Multiple Immunization
- NATIONAL INSTITUTES OF HEALTH
- 1951-- Consultant to National Institutes of Health
- U.S. GOVERNMENT
- 1973-- Consultant to Bureau of Biologics, Food and Drug Administration
- 1973-- Member, FDA Bureau of Biologics Panel on Review of Viral  
Vaccines and Rickettsial Vaccines
- 1974-- MEMBER, Environmental Measurements Advisory Committee,  
Science Advisory Board, U.S. Environmental Protection Agency
- WORLD HEALTH ORGANIZATION
- 1949-- Member, Regional Laboratory, Influenza Study Program  
(Director 1949--)
- 1951-- Member, Expert Advisory Panel on Virus Diseases
- 1971-- Member, Scientific Advisory Committee to the World Health  
Organization, East African Virus Research Institute,  
Entebbe, Uganda
- 1975-- Member, Scientific Group on Virus Diseases  
(Member 1966)

PRESENT  
APPOINTMENTS  
(continued)

## MISCELLANEOUS

- 1949-65 American Type Culture Collection  
Member, Viral and Rickettsial Registry
- 1971-76 East African Virus Research Institute, Entebbe, Uganda  
Consultant to the Institute
- 1973-77 American Board of Medical Microbiology  
Member, Virology Standards and Examination Committee
- 1973- American Public Health Association  
Member, Committee on Laboratory Standards and Practices  
(Member 1964-1971)
- 1975- American Water Works Association  
Member, Viruses in Water Committee
- 1978- Tissue Culture Association, Inc.  
Past President  
(President 1976-1978)  
(First Vice President 1973-1975)
- 1978- American Society for Microbiology  
President  
(Vice President 1977)
- 1978- Peralta Cancer Research Institute, Peralta Hospital,  
Oakland, California  
Member, Board of Directors and President of the Board, 1985-
- 1970- Member, Board of Directors, California Public Health  
Foundation and President of the Foundation, 1980-
- 1978- Consultant, Cetus Corporation
- 1982- Consultant, Chiron Corporation
- 1985- President, Virion, (U.S.) Inc.

## EDITORSHIPS

- 1963-- Proceedings of the Society for Experimental Biology and Medicine,  
Member, Editorial Board
- 1965-- American Journal of Epidemiology  
(Formerly American Journal of Hygiene: 1959-1962, 1964-1965)  
Member, Editorial Board
- 1970-- Infection and Immunity  
Member, Editorial Board
- 1972-85 Intervirology  
Section Editor of Epidemiology
- 1975-- Methods in Virology  
Member, Board of Advisors
- 1976-- Infection  
Member, Editorial Board
- 1978-- Journal of Medical Virology  
Member, Editorial Board

## EDWIN H. LENNETTE

PROFESSIONAL  
SOCIETIES

- 1947-83 Alameda-Contra Costa Medical Association
- 1958-- American Academy of Microbiology (Charter Member)
- 1954-56 American Academy of Tropical Medicine (Dissolved 1956)
- 1945-- American Association for the Advancement of Science (Fellow)
- 1963-76 American Association for Cancer Research
- 1939-- American Association of Immunologists (Emeritus Member 1974)
- 1941-- American Association of Pathologists and Bacteriologists  
(Emeritus Member 1975)
- 1968-73 American Biology Council (Founding Member) (Dissolved 1973)
- 1954-- American Epidemiological Society (Emeritus Member 1972)
- 1961-77 American Public Health Association (Fellow)
- 1948-61 American Public Health Association, Western Branch
- 1940-- American Society for Experimental Pathology
- 1933-- American Society for Microbiology  
(Formerly Society of American Bacteriologists)
- 1972-- American Society of Clinical Pathologists (Honorary Fellow 1972)
- 1945-- American Society of Tropical Medicine and Hygiene
- 1972-- Bay Area Infectious Disease Society
- 1958-- Belgian Society of Tropical Medicine (Foreign Corresponding  
Member)
- 1959-62 California Academy of Preventive Medicine
- 1948- 83 California Medical Association
- 1940-- Harvey Society (Emeritus Member 1973)
- 1958-- Hollywood Academy of Medicine
- 1943-81 Royal Society of Tropical Medicine and Hygiene (Fellow)  
(Emeritus Member, 1981)
- 1939-- Society for Experimental Biology and Medicine
- 1970-81 Society for General Microbiology  
(Emeritus Member, 1981)

## EDWIN H. LENNETTE

PROFESSIONAL  
SOCIETIES  
(continued)

- 1948-- Tissue Culture Association, Inc. (Emeritus Member)  
 1959-- Western Association of Physicians (Emeritus Member 1974)  
 1951-- Western Society for Clinical Research (Emeritus Member 1966)  
 1981-- American Society for Rickettsiology and Rickettsial Diseases

PAST TEACHING  
APPOINTMENTS

- 1947-58 Lecturer in Bacteriology, Department of Bacteriology,  
 University of California, Berkeley

PAST  
APPOINTMENTS

## AMERICAN TYPE CULTURE COLLECTION

- 1960-63 Member, Council of the Viral and Rickettsial Registry  
 1972-74 Member, Sponsoring Societies Committee of ATCC  
 Development Program

## CALIFORNIA NATIONAL CENTER FOR PRIMATE BIOLOGY

- 1967-69 Member, Advisory Committee

## CENTER FOR DISEASE CONTROL, PUBLIC HEALTH SERVICE

- 1950-62 Consultant, Communicable Disease Center, Laboratory Branch  
 1968-72 Member, Medical Laboratory Services Advisory Committee  
 1976-77 Member, Drinking Water Disinfection Ad Hoc Advisory Committee

COMMISSION ON UNDERGRADUATE EDUCATION IN THE  
BIOLOGICAL SCIENCES

- 1968-69 Member of the Commission

## DEPARTMENT OF DEFENSE

- 1948-56 Member, Advisory Panel  
 Naval Biological Laboratory  
 1948-73 Member, Commission on Influenza  
 Armed Forces Epidemiological Board  
 Office of The Surgeon General, Department of the Army  
 (Associate Member 1948-1951)  
 (Commission dissolved 1973)

PAST  
APPOINTMENTS  
(continued)

DEPARTMENT OF DEFENSE (continued)

- 1951-73 Member, Commission on Rickettsial Diseases  
Armed Forces Epidemiological Board  
Office of The Surgeon General, Department of the Army  
(Advisory Member 1971-1973)  
(Commission dissolved 1973)
- 1970-76 Member, Armed Forces Epidemiological Board  
Office of The Surgeon General, Department of the Army  
(President 1973-1976)

DEPARTMENT OF STATE

- 1970-76 Member, U.S. Delegation, U.S.-Japan Cooperative Medical  
Science Program

NATIONAL ACADEMY OF SCIENCES--NATIONAL RESEARCH COUNCIL

- 1976-77 Member, Margin of Safety and Extrapolation Subcommittee,  
Safe Drinking Water Committee

NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE

- 1951-56 Coordinator, Section XII, Sectional Research Program
- 1965-69 Member and Chairman, Panel on Viral Diseases  
U.S.-Japan Cooperative Medical Science Program  
Office of Science and Technology  
The White House and the Office of International Research

NIH, DIVISION OF RESEARCH GRANTS AND FELLOWSHIPS

- 1951-53 Member, Virus and Rickettsial Study Section  
(Chairman 1952-1953)
- 1953-56 Member, Microbiology and Immunology Study Section  
(Co-Chairman 1953-1954) (Chairman 1955-1956)

NIH, NATIONAL CANCER INSTITUTE

- 1966-72 Member, Solid Tumor Virus Segment  
Special Virus Cancer Program
- 1967-73 Consultant to the National Cancer Institute

## EDWIN H. LENNETTE

PAST  
APPOINTMENTS  
(continued)

## NIH, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

- 1957-61 Chairman of the Board of Scientific Counselors
- 1960-62 Member, Allergy and Infectious Diseases Training Grant Committee  
(Chairman 1962)
- 1960-63 Member, Panel for Respiratory and Related Viruses
- 1963-66 Member, National Advisory Allergy and Infectious Disease Council
- 1963-68 Member, Committee for Vaccine Development  
(Chairman 1967-1968)
- 1965-66 Member and Chairman, Subcommittee on Rubella Virus

## NIH, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS

- 1963-64 Chairman, Ad Hoc Committee for Rubella Vaccine

## THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS

- 1953-54 Member, Advisory Committee  
Poliomyelitis Vaccine Evaluation Center

## THE WHITE HOUSE

- 1964 Member, Microbiology Panel, Wooldridge Committee

## WORLD HEALTH ORGANIZATION

- 1952-62 Member, Expert Advisory Panel on Zoonoses

## MISCELLANEOUS

- 1966-77 The University of Texas at Houston, M.D. Anderson Hospital and Tumor Institute  
Consultant in Clinical and Diagnostic Virology
- 1976-77 Frederick Cancer Research Center  
Member, Cancer Research Safety Symposia Planning Committee

PAST  
APPOINTMENTS  
(continued)

- 1975-82 Leonard Wood Memorial  
Member, Scientific Advisory Board
- 1978-83 The Christ Institute of Medical Research, Cincinnati, Ohio  
Consultant to the Institute

## EDWIN H. LENNETTE

PAST  
PROFESSIONAL  
SOCIETIES  
OFFICERSHIPS

## AMERICAN ACADEMY OF MICROBIOLOGY

- 1960-66 Member, Board of Governors  
(Vice Chairman 1963-1965)
- 1960-65 Member, Standards and Examination Committee for  
Certification in Public Health and Medical Laboratory  
Virology
- 1967-72 Member, Committee on Elections  
(Chairman 1972)
- 1971-73 Member, Committee on Ethics

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE  
(Representing the American Society for Experimental  
Pathology)

- 1964-66 Member of the Council, Section N. - Medical Sciences

## AMERICAN ASSOCIATION OF IMMUNOLOGISTS

- 1961-67 Member of the Council
- 1966-67 President of the Association

## AMERICAN BIOLOGY COUNCIL

- 1968-70 Member (Founding Member)  
(Chairman 1969-1970)

## AMERICAN CANCER SOCIETY

- 1963-66 Member, Advisory Committee on Research on the Etiology  
of Cancer  
(Vice Chairman 1964-1965) (Chairman 1965-1966)

## AMERICAN EPIDEMIOLOGICAL SOCIETY

- 1970-71 Vice President of the Society

## AMERICAN SOCIETY FOR MICROBIOLOGY

- 1978-79 President of the Society

## TISSUE CULTURE ASSOCIATION

- 1976-78 President of the Association

PAST  
PROFESSIONAL  
SOCIETIES  
OFFICERSHIPS  
(continued)

AMERICAN SOCIETY FOR MICROBIOLOGY  
(Formerly Society of American Bacteriologists)

- 1949-53 Member of the Council  
1974-75 Committee member, Wyeth Award in Clinical Microbiology

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE

- 1951-55 Member of the Council

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY

- 1960-61 Member, Microbiology Panel, Study on Manpower Needs  
in the Basic Health Sciences  
1967-69 Member of the Board and Executive Committee  
(Chairman 1968-1969)  
1968-69 President of the Federation

THE HASTINGS FOUNDATION, LOS ANGELES

- 1966-76 Member, Scientific Advisory Committee

PAST  
EDITORSHIPS

- 1951-54 The Journal of Bacteriology  
Member, Editorial Board  
1951-57 The American Journal of Tropical Medicine and Hygiene  
Member, Editorial Board  
1960-63 The Journal of Infectious Diseases  
Advisory Editor  
The Journal of Immunology  
1960-68 Associate Editor  
1968-71 Member, Editorial Board  
1964-69 Alameda-Contra Costa Medical Association Bulletin  
Member, Editorial Board  
1970-74 Biomedical News  
Member, Editorial Advisory Board  
(Publication discontinued with January 1974 issue)  
1971-77 Excerpta Medica (Section on Virology)  
Member, Editorial Board

## EDWIN H. LENNETTE

BOOKS EDITED  
OR CHAPTERS  
CONTRIBUTED  
TO BOOKS

1. Lennette, Edwin H., 1950. Immunity in viral diseases. Pages 37-51 in Cyclopedia of medicine, surgery and specialties, Volume 7. F. A. Davis Company, Philadelphia.
2. Railsback, O.C. and Lennette, Edwin H., 1950. Q fever, method of. Pages 32-33 in Current therapy. W. B. Saunders and Company, Philadelphia.
3. Lennette, Edwin H. and Clark, William H., 1950. Q fever (Queensland fever; Balkan grippe). Pages 883-895 in Nelson's Loose-leaf medicine, perpetual system of living medicine, Volume I. Thomas Nelson and Sons, New York.
4. Railsback, O.C. and Lennette, Edwin H., 1951. Q fever, method of. Pages 29-30 in Current therapy. W. B. Saunders and Company, Philadelphia.
5. Lennette, Edwin H., 1951. Interference between animal viruses. Pages 277-294 in Annual review of microbiology. George Banta Publishing Company, Stanford.
6. Lennette, Edwin H., 1951. Yellow fever. Pages 1027-1040 in Cyclopedia of medicine, surgery and specialties, Volume 14. F. A. Davis Company, Philadelphia.
7. Lennette, Edwin H., 1954. An evaluation of diagnostic procedures for virus and rickettsial diseases. Pages 348-371 in The dynamics of virus and rickettsial infections. The Blakiston Company, Inc., New York.
8. Lennette, Edwin H., 1954. Immunity in viral diseases. Pages 37-52G in Cyclopedia of medicine, surgery and specialties, Volume 7. F. A. Davis Company, Philadelphia.
9. Lennette, Edwin H., 1956. Q fever. Pages 469-473 in Meakins' Practice of medicine, 6th ed. The C. V. Mosby Company, St. Louis.
10. Lennette, Edwin H., 1956. General principles underlying laboratory diagnosis of virus and rickettsial infections. Pages 1-52 in Diagnostic procedures for virus and rickettsial diseases, 2d ed. American Public Health Association, New York.
11. Lennette, Edwin H., 1958. Arthropod-borne viral encephalitides. Epidemiology of Western Equine and St. Louis encephalitis. Pages 22-42 in Viral encephalitis. A symposium, fifth annual scientific meeting of the Houston Neurological Society, Texas Medical Center, Houston, Texas. Charles C. Thomas, Springfield

BOOKS EDITED  
OR CHAPTERS  
CONTRIBUTED  
TO BOOKS  
(continued)

12. Lennette, Edwin H., 1958. Viral infections of the upper respiratory tract. Trans. Amer. Acad. Ophthalmology and Otolaryngology. Section on symposium: Viruses and viral diseases (May-June):399-410.
13. Lennette, Edwin H., 1958. Problems of the viral diagnostic laboratory with respect to poliomyelitis. Pages 377-386 in Poliomyelitis. Papers and discussions presented at the Fourth international poliomyelitis conference. J. P. Lippincott Company, Philadelphia.
14. Lennette, Edwin H., 1959. Q fever. Pages 880-895 in Viral and rickettsial infections of man, 3d ed. J. P. Lippincott Company, Philadelphia.
15. Lennette, Edwin H., 1959. Serologic reactions in viral and rickettsial infections. Pages 230-250 in Viral and rickettsial infections of man, 3d. ed. J. P. Lippincott Company, Philadelphia.
16. Lennette, Edwin H., 1959. Psittacosis (Ornithosis), method of. Page 34 in Current therapy, 11th ed. W. B. Saunders Company, Philadelphia.
17. Lennette, Edwin H., 1960. Psittacosis (Ornithosis), method of. Pages 38-39 in Current therapy, 12th ed. W. B. Saunders Company, Philadelphia.
18. Lennette, Edwin H., 1960. Q fever. Page 808 in Encyclopaedia Britannica, Inc., Volume 18. William Benton, Chicago.
19. Schmidt, Nathalie J. and Lennette, Edwin H., 1961. Recent advances in the serodiagnosis of virus infections. Pages 1-58 in Progress in medical virology, Volume 3. Karger, Basel, New York.
20. Lennette, Edwin H., 1964. General principles underlying laboratory diagnosis of viral and rickettsial infections. Pages 1-66 in Diagnostic procedures for viral and rickettsial diseases, 3d ed. The American Public Health Association, Inc., New York.
21. Schmidt, Nathalie J. and Lennette, Edwin H., 1965. Basic technics for virology. Pages 1189-1231 in Viral and rickettsial infections of man, 4th ed. J. P. Lippincott Company, Philadelphia.
22. Sanders, Murray and Lennette, Edwin H., ed. 1965. Applied virology. Proceedings of the first annual symposium on applied virology. Olympic Press, Inc., Wisconsin. 319 pp.

## EDWIN H. LENNETTE

BOOKS EDITED  
OR CHAPTERS  
CONTRIBUTED  
TO BOOKS  
(continued)

23. Schmidt, Nathalie J. and Lennette, Edwin H., 1967. The preparation of animal viruses for use as antigens. Pages 87-102 in Methods in immunology and immunochemistry, Volume 1. Academic Press, Inc., New York.
24. Sanders, Murray and Lennette, Edwin H., ed. 1968. Medical and applied virology. Proceedings of the second international symposium. Warren H. Green, Inc., St. Louis. 405 pp.
25. Lennette, Edwin H. and Schmidt, Nathalie J., ed. 1969. Diagnostic procedures for viral and rickettsial infections, 4th ed. American Public Health Association, Inc., New York. 978 pp.
26. Lennette, Edwin H., 1969. General principles underlying laboratory diagnosis of viral and rickettsial infections. Pages 1-65 in Diagnostic procedures for viral and rickettsial infections, 4th ed. American Public Health Association, Inc., New York.
27. Lennette, Edwin H., 1970. Discussion of preceding papers. Unusual isolates from clinical material. Annals of the New York Acad. of Sciences, New York, October 30. Volume 174, Article 2:999-1005.
28. Blair, John E., Lennette, Edwin H. and Truant, Joseph P., ed. 1970. Manual of clinical microbiology, 1st ed. American Society for Microbiology, Bethesda. 727 pp.
29. Lennette, Edwin H., Melnick, Joseph L. and Chanock, Robert M., 1970. Clinical virology: introduction to methods. Pages 489-497 in Manual of clinical microbiology, 1st ed. American Society for Microbiology, Bethesda.
30. Pollard, Morris and Lennette, Edwin H., ed. 1971. Epilog. Pages 297-307 in Perspectives in virology VII, from molecules to man. Academic Press, New York.
31. Lennette, Edwin H. and Emmons, Richard W., 1971. The laboratory diagnosis of rabies, review and prospective. Pages 77-90 in Rabies, proceedings of working conference on rabies, Tokyo, 1970. University Park Press, Baltimore.
32. Lennette, E. H. and Emmons, Richard W., 1972. Health problems associated with the transportation and use of nondomestic animals: an overview. Proceedings of the II International symposium on health aspects of the international movement of animals. Pan American Health Organization, pages 3-9. (Scientific Publication No. 235)

BOOKS EDITED  
OR CHAPTERS  
CONTRIBUTED  
TO BOOKS  
(continued)

33. Hull, R.M., Dwyer, A.C., Holmes, A.W., Nowakowski, E., Deinhardt, F., Lennette, E.H., and Emmons, R.W., 1972. Recovery and characterization of a new simian herpesvirus from a fatally infected spider monkey. Proceedings of the II International symposium on health aspects of the international movement of animals. Pan American Health Organization, pages 137-144. (Scientific Publication No. 235)
34. Schmidt, Nathalie J. and Lennette, Edwin H., 1972. Complement fixation tests for detection of antigen and antibody associated with viral hepatitis, type B. Pages 125-132 in Girish N. Vyas, Herbert A. Perkins, and Rudi S. Schmid, eds. Hepatitis and blood transfusion. Grune & Stratton, Inc., New York.
35. Lennette, Edwin H., 1973. Neutralization, fluorescent antibody and complement fixation tests for rubella. Pages 18-32 in Herman Friedman and James E. Prior, eds. Rubella. Charles C. Thomas, Springfield.
36. Lennette, Edwin H., 1973. Potential hazards posed by non-viral agents. Pages 47-62 in A. Hellman, M. N. Oxman, and R. Pollack, eds. Biohazards in biological research. Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.
37. Lennette, Edwin H. and Schmidt, Nathalie J., 1973. Principles and performance of the rubella hemagglutination inhibition test. Commission on continuing education council on microbiology. American Society of Clinical Pathologists, Chicago. 32 pp.
38. Lennette, Edwin H. and Schmidt, Nathalie J., 1973. Serodiagnosis of viral infections. Chapter V, International congress series No. 285, Anatomic and clinical pathology. Proceedings of the VIII World congress of anatomic and clinical pathology, Munich, September 12-16, 1972. Excerpta Medica, Amsterdam, pages 168-171.
39. Zeman, Wolfgang and Lennette, Edwin H., ed., 1974. Slow virus diseases. Williams & Wilkins Company, Baltimore. 145 pp
40. Lennette, Edwin H., Spaulding, Earle H., and Truant, Joseph P., ed. Manual of clinical microbiology, 2d ed. American Society for Microbiology, Washington, D.C. 970 pp.
41. Lennette, Edwin H., 1975. Perspectives in virology: vaccinations. Pages 1-8 in Perspectives in virology IX, Antiviral mechanisms. M. Pollard, ed. Academic Press, New York.

## EDWIN H. LENNETTE

BOOKS EDITED  
OR CHAPTERS  
CONTRIBUTED  
TO BOOKS  
(continued)

42. Lennette, Edwin H., 1975. Introduction to Section IV. New vaccines. Page 399 in David Schlessinger, ed. Microbiology-1975. American Society for Microbiology, Washington, D.C.
43. Lennette, E.H. and McManus, J.F.A., 1975. Chapter I. Introduction. Pages 1-13 in K.D. Fisher and A.U. Nixon, ed. The science of life: contributions of biology to human welfare. Plenum Press, New York.
44. Berg, Gerald, Bodily, Howard L., Lennette, Edwin H., Melnick, Joseph L. and Metcalf, Theodore G., ed. 1976. Viruses in water, American Public Health Association, Inc., Washington, D.C. 256 pp.
45. Lennette, Edwin H., 1976. Part VI. Perspectives: An appraisal of need. Epidemiology. Page 252 in Viruses in water. American Public Health Association, Inc., Washington, D.C.
46. Lennette, Edwin H. Keynote address: Problems posed to man by viruses in municipal wastes. Pages 1-7 in Baldwin, L.B., Davidson, J.M., and Gerber, J.F., ed. 1977. Virus aspects in applying municipal waste to land. University of Florida, Gainesville, Florida.
47. Lennette, Edwin H. and Schmidt, Nathalie J., ed. 1979. Diagnostic procedures for viral, rickettsial and chlamydial infections, 5th ed. American Public Health Association, Inc., Washington, D.C.
48. Lennette, Edwin H., Balows, Albert, Hausler, William J, Jr. and Truant, Joseph P., ed. 1980. Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.
49. Lennette, Edwin H. and Schmidt, Nathalie J., 1983. Newer methods for the detection of primate viruses. Pp. 149-160 in Viral and Immunological Diseases in Nonhuman Primates. Monographs in Primatology, Vol. 2. Kalter, S.S., ed. Alan R. Liss, Inc., New York.
50. Lennette, Edwin H., Balows, Albert, Hausler, William Jr., Jr. and Shadomy, H. Jean, ed. 1985. Manual of clinical microbiology, 4th ed. American Society for Microbiology, Washington, D.C.
51. Lennette, Edwin H., ed. 1985. Laboratory diagnosis of viral infections. Marcel Dekker, Inc., New York and Basel.

APPENDIX B  
BIBLIOGRAPHY

Edwin H. Lennette

1. The Examination of Pooled Human-Serum for its Neutralizing Effect on the Poliomyelitis Virus.  
 Hudson, N. Paul and Lennette, Edwin H.  
 Jour. Prev. Med., 1932, 6 (4), 335-339 (July)
2. Neutralization of Poliomyelitis Virus by the Serum of Liberian Negroes.  
 Hudson, N. Paul and Lennette, Edwin H.  
 Proc. Soc. Exper. Biol. and Med., 1932, 29 (9), 1090-1091 (June)
3. Neutralization of Poliomyelitis Virus by the Serum of Native Chinese of Peiping.  
 Lennette, Edwin H. and Hudson, N. Paul  
 Proc. Soc. Exper. Biol. and Med., 1933, 30 (4), 449-451 (Jan.)
4. The Neutralization of Poliomyelitis Virus by the Serum of Liberian Negroes.  
 Hudson, N. Paul and Lennette, Edwin H.  
 Amer. Jour. Hyg., 1933, 17 (3), 581-586 (May)
5. Failure to Neutralize the Poliomyelitis Virus with Sera of Adult Macacus Rhesus and of Young Female Rhesus Treated with Anterior Pituitary Extracts.  
 Hudson, N. Paul, Lennette, Edwin H. and King, Ernest Q.  
 Jour. Exper. Med., 1934, 59 (5), 543-552 (May)
6. Relation of Olfactory Tracts to Intravenous Route of Infection in Experimental Poliomyelitis.  
 Lennette, Edwin H. and Hudson, N. Paul  
 Proc. Soc. Exper. Biol. and Med., 1935, 32 (9), 1444-1446 (June)
7. Failure to Infect Monkeys with Poliomyelitis Virus Through Isolated Intestinal Loops.  
 Lennette, Edwin H. and Hudson, N. Paul  
 Jour. Infect. Dis., 1936, 58 (1), 10-14 (Jan.-Feb.)

Bibliography  
Edwin H. Lennette

8. Blood-CNS Barrier in Experimental Poliomyelitis.  
Lennette, Edwin H. and Hudson, N. Paul  
Proc. Soc. Exper. Biol. and Med., 1936, 34 (4), 470-472 (May)
9. Factors of Resistance in Experimental Poliomyelitis. With Comments on Immunity in Poliomyelitis.  
Hudson, N. Paul, Lennette, Edwin H. and Gordon, Francis B.  
J.A.M.A., 1936, 106 (24), 2037-2042 (June 13)
10. Permeability of Blood-CNS Barrier in Experimental Poliomyelitis as Determined by the Nitrate Test.  
Lennette, Edwin H. and Reames, Harold R.  
Proc. Soc. Exper. Biol. and Med., 1937, 36 (5), 769-770 (June)
11. Permeability of the Blood-C. N. S. Barrier to Sodium Bromide in Experimental Poliomyelitis.  
Lennette, Edwin H. and Campbell, Dan H.  
Science, 1937, 86 (2224), 160 (Aug. 13)
12. Studies on the Role of the Spleen in Experimental Poliomyelitis.  
Lennette, Edwin H.  
Jour. Exper. Med., 1937, 66 (5), 549-564 (Nov.)
13. Incidence of Poliocidal Sera in Regions Where Poliomyelitis Epidemics are Infrequent.  
Hudson, N. Paul and Lennette, Edwin H.  
Amer. Jour. Trop. Med., 1938, 18 (1), 35-40 (Jan.)
14. Further Studies on the Permeability to Sodium Nitrate of the Blood-CNS Barrier in Experimental Poliomyelitis.  
Lennette, Edwin H. and Reames, Harold R.  
Jour. Immunol., 1938, 34 (3), 215-220 (Mar.)

Bibliography  
Edwin H. Lennette

15. Fermeability of Blood-CNS Barrier to Sodium Bromide in Experimental Poliomyelitis.  
Lennette, Edwin H. and Campbell, Dan H.  
Amer. Jour. Dis. Child., 1938, 56, 756-763 (Oct.)
16. Nitrate and Bromide Tests for Blood-CNS Barrier Fermeability in Experimental Poliomyelitis.  
Lennette, Edwin H., Campbell, Dan H. and Reames, Harold R.  
Proc. Soc. Exper. Biol. and Med., 1939, 40 (2), 287-289 (Feb.)
17. The Blood Stream in Experimental Poliomyelitis.  
Gordon, F. B. and Lennette, Edwin H.  
Jour. Infect. Dis., 1939, 64 (2), 97-104 (Mar.-Apr.)
18. The Propagation of St. Louis Encephalitis Virus in Mouse Testicle.  
Lennette, Edwin H. and Smith, Margaret G.  
Proc. Soc. Exper. Biol. and Med., 1939, 41 (1), 193-194 (May)
19. Blood-CNS Barrier Permeability to Horse Serum in Experimental Poliomyelitis.  
Lennette, Edwin H. and Campbell, Dan H.  
Proc. Soc. Exper. Biol. and Med., 1939, 41 (2), 320-323 (June)
20. Comparison of Activity of Viruses of St. Louis and Japanese Encephalitis in the Chick Embryo.  
Smith, M. G. and Lennette, E. H.  
Proc. Soc. Exper. Biol. and Med., 1939, 41 (2), 323-326 (June)
21. On the Relationship Between Humoral and Tissue Immunity in Experimental Poliomyelitis.  
Lennette, Edwin H. and Hudson, N. Paul  
Jour. Infect. Dis., 1939, 65, 78-83 (July-Aug.)

Bibliography  
Edwin H. Lennette

22. Preservation of St. Louis Encephalitis Virus.  
Lennette, Edwin H. and Smith, Margaret G.  
Jour. Infect. Dis., 1939, 65, 252-254 (Nov.-Dec.)
23. Etiologic Studies of Sporadic Cases of Encephalitis Occurring in the St. Louis Area in 1938.  
Smith, Margaret G., Lennette, Edwin H. and Blattner, Russell J.  
Amer. Jour. Dis. Child., 1940, 59, 509-514 (Mar.)
24. Propagation of the St. Louis and the Japanese B Encephalitis Viruses in Mouse Testicle.  
Lennette, Edwin H. and Smith, Margaret G.  
Jour. Infect. Dis., 1940, 66, 266-270 (May-June)
25. A Complex Vaccine Effective Against Different Strains of Influenza Virus.  
Horsfall, Frank L., Jr. and Lennette, Edwin H.  
Science, 1940, 91 (2369), 492-494 (May 24)
26. Electrophoresis of the Complement-Fixing Antigen of Human Influenza Virus.  
Bourdillon, Jaques and Lennette, Edwin H.  
Jour. Exper. Med., 1940, 72 (1), 11-19 (July)
27. Studies on Epidemic Influenza Virus. The Nature and Properties of the Complement-Fixing Antigen.  
Lennette, Edwin H. and Horsfall, Frank L., Jr.  
Jour. Exper. Med., 1940, 72 (3), 233-246 (Sept.)
28. The Synergism of Human Influenza and Canine Distemper Viruses in Ferrets.  
Horsfall, Frank L., Jr. and Lennette, Edwin H.  
Jour. Exper. Med., 1940, 72 (3), 247-259 (Sept.)

Bibliography  
Edwin H. Lennette

29. The Nomenclature of Influenza.  
Horsfall, F. L., Jr., Lennette, E. H., Rickard, E. R.,  
Andrewes, C. H., Smith, Wilson and Stuart-Harris, C. H.  
Lancet, 1940, 2, 413-414 (Oct. 5)
30. A Comprehensive Study of Influenza in a Rural Community.  
Rickard, E. R., Lennette, Edwin H. and Horsfall, Frank L., Jr.  
Pub. Hlth. Rep., 1940, 55 (47), 2146-2167 (Nov. 22)
31. Isolation of the Virus of Herpes Simplex and the Demonstration of  
Intranuclear Inclusions in a Case of Acute Encephalitis.  
Smith, Margaret G., Lennette, Edwin H. and Reames, Harold R.  
Amer. Jour. Path., 1941, 17 (1), 55-68 (Jan.)
32. Neutralization of Influenza A Virus by Human Serum.  
Horsfall, Frank L., Jr. and Lennette, Edwin H.  
Jour. Exper. Med., 1941, 73 (3), 327-333 (Mar.)
33. A Complex Vaccine Against Influenza A Virus. Quantitative Analysis  
of the Antibody Response Produced in Man.  
Horsfall, Frank L., Jr., Lennette, Edwin H. and Rickard, Elsmere R.  
Jour. Exper. Med., 1941, 73 (3), 335-355 (Mar.)
34. Studies on Influenza Virus. The Complement-Fixing Antigen of  
Influenza A and Swine Influenza Viruses.  
Lennette, Edwin H. and Horsfall, Frank L., Jr.  
Jour. Exper. Med., 1941, 73 (5), 581-599 (May)
35. Susceptibility of Syrian Hamster (Cricetus auratus) to Viruses  
of St. Louis and Japanese B Encephalitis.  
Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1941, 47 (1), 178-181 (May)

Bibliography  
Edwin H. Lennette

36. The Diverse Etiology of Epidemic Influenza.  
Lennette, E. H., Rickard, E. R., Hirst, G. K. and  
Horsfall, F. L., Jr.  
Pub. Hlth. Rep., 1941, 56 (36), 1777-1788 (Sept. 5)
37. The Correlation Between Neutralizing Antibodies in Serum Against  
Influenza Viruses and Susceptibility to Influenza in Man.  
Rickard, E. R., Horsfall, F. L., Jr., Hirst, G. K. and  
Lennette, E. H.  
Pub. Hlth. Rep., 1941, 56 (37), 1819-1834 (Sept. 12)
38. Studies on the Efficacy of a Complex Vaccine Against Influenza A.  
Horsfall, F. L., Jr., Lennette, E. H., Rickard, E. R. and Hirst, G. K.  
Pub. Hlth. Rep., 1941, 56 (38), 1863-1875 (Sept. 19)
39. Encephalitis in Man Following Vaccination with 17 D Yellow Fever Virus.  
Fox, John P., Lennette, Edwin H., Manso, Caio and  
Souza Aguiar, Jacy R.  
Amer. Jour. Hyg., 1942, 36 (2), 117-142 (Sept.)
40. Anticorpos Neutralizantes para a Amostra Leste do Virus de  
Encefalomyelite Equina em Equideos no Brasil.  
Lennette, Edwin H. and Fox, John P.  
Mem. Inst. Oswaldo Cruz, 1943, 38 (1), 85-92 (Feb.)
41. The Complement Fixation Test in the Diagnosis of Yellow Fever.  
Use of Infectious Mouse Brain as Antigen.  
Lennette, Edwin H. and Perlowagora, Alina  
Amer. Jour. Trop. Med., 1943, 23 (5), 481-504 (Sept.)
42. Recent Advances in Viruses. A Brief Survey of Recent Work on  
Viruses and Virus Diseases.  
Lennette, Edwin H.  
Science, 1943, 98 (2550), 415-423 (Nov. 12)

## Bibliography

Edwin H. Lennette

43. Human Infection with Venezuelan Equine Encephalomyelitis Virus. A Report on Eight Cases of Infection Acquired in the Laboratory.  
Lennette, Edwin H. and Koprowski, Hilary  
J.A.M.A., 1943, 123 (17), 1088-1095 (Dec. 25)
44. Propagation of Yellow Fever Virus in Tissue Cultures Containing Sulfonamides.  
Koprowski, Hilary and Lennette, Edwin H.  
Amer. Jour. Hyg., 1944, 40 (1), 1-13 (July)
45. Sulfonamides in Yellow Fever Virus Infections of Mice and Developing Chick Embryos.  
Koprowski, Hilary and Lennette, Edwin H.  
Amer. Jour. Hyg., 1944, 40 (1), 14-25 (July)
46. Observations on the Possible Usefulness of the Complement-Fixation Test in the Early Diagnosis of Yellow Fever.  
Perlowagora, Alina and Lennette, Edwin H.  
Amer. Jour. Trop. Med., 1944, 24 (4), 235-244 (July)
47. Influence of Age on the Susceptibility of Mice to Infection with Certain Neurotropic Viruses.  
Lennette, Edwin H. and Koprowski, Hilary  
Jour. Immunol., 1944, 49 (3), 175-191 (Sept.)
48. Pathogenesis of Venezuelan Equine Encephalomyelitis Virus Infections in the Developing Chick Embryo.  
Koprowski, Hilary and Lennette, Edwin H.  
Jour. Bact., 1944, 48 (4), 463-472 (Oct.)
49. Neutralization Tests with Certain Neurotropic Viruses. A Comparison of the Sensitivity of the Extraneural and Intracerebral Routes of Inoculation for the Detection of Antibodies.  
Lennette, Edwin H. and Koprowski, Hilary  
Jour. Immunol., 1944, 49 (6), 375-385 (Dec.)

Bibliography  
Edwin H. Lennette

50. The Complement Fixation Test in the Diagnosis of Yellow Fever. Comparative Value of the Serologic and Histopathologic Methods of Diagnosis.  
Lennette, Edwin H. and Perlowagora, Alina  
Amer. Jour. Trop. Med., 1945, 25 (1), 11-18 (Jan.)
51. Serologic Distinctness of Eastern, Western, and Venezuelan Equine Encephalomyelitis Viruses.  
Lennette, Edwin H. and Koprowski, Hilary  
Proc. Soc. Exper. Biol. and Med., 1945, 60, 110-114 (Oct.)
52. Laboratory Diagnosis of Encephalitis.  
Lennette, Edwin H.  
California's Health, 1945, 3 (9), 33-34 (Nov. 15)
53. The Comparative Sensitivity of Venezuelan Equine Encephalomyelitis Virus Neutralization Tests in Chick Embryos and in Mice.  
Koprowski, Hilary and Lennette, Edwin H.  
Jour. Bact., 1946, 51 (2), 257-261 (Feb.)
54. Antigenic Relationships of the West Nile, Japanese B Encephalitis, and St. Louis Encephalitis Viruses.  
Lennette, Edwin H. and Koprowski, Hilary  
Jour. Immunol., 1946, 52 (3), 235-246 (Mar.)
55. Interference Between Viruses in Tissue Culture.  
Lennette, Edwin H. and Koprowski, Hilary  
Jour. Exper. Med., 1946, 83 (3), 195-219 (Mar.)
56. Neurosecretion. IX. Cytoplasmic Inclusions in Peripheral Autonomic Ganglion Cells of the Monkey.  
Lennette, Edwin H. and Scharrer, Ernst  
The Anatomical Record, 1946, 94 (1), 85-92 (Jan.)

Bibliography  
Edwin H. Lennette

57. Isolation of St. Louis Encephalitis Virus from a Fatal Human Case in California.  
Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1946, 61 (3), 206-210 (Mar.)
58. Comparative Sensitivity of the Extraneural and Intracerebral Neutralization Tests in Following the Antibody Response in Man to Vaccination with Western Equine Encephalomyelitis Virus.  
Lennette, Edwin H. and Koprowski, Hilary  
Jour. Immunol., 1946, 52 (4), 343-353 (Apr.)
59. Effect of In Vitro Cultivation on the Pathogenicity of West Nile Virus.  
Koprowski, Hilary and Lennette, Edwin H.  
Jour. Exper. Med., 1946, 84 (2), 181-190 (Aug.)
60. Effect of In Vitro Cultivation on the Pathogenicity of Venezuelan Equine Encephalomyelitis Virus.  
Koprowski, Hilary and Lennette, Edwin H.  
Jour. Exper. Med., 1946, 84 (3), 205-210 (Sept.)
61. Q Fever in California.  
Lennette, Edwin H.  
Calif. Med., 1948, 69 (2), 91-95 (Aug.)
62. Q Fever in Central and Northern California.  
Lennette, Edwin H. and Meiklejohn, Gordon  
Calif. Med., 1948, 69 (3), 197-199 (Sept.)
63. Treatment of Q Fever in Man with Aureomycin.  
Lennette, E. H., Meiklejohn, G. and Thelen, H. M.  
Ann. N.Y. Acad. Sci., 1948, 51 (Art. 2), 331-342 (Nov. 30)
64. Sheep and Goats in the Epidemiology of Q Fever in Northern California.  
Lennette, Edwin H., Clark, William H. and Deen, Ben H.  
Amer. Jour. Trop. Med., 1949, 29 (4), 527-541 (July)

Bibliography  
Edwin H. Lennette

65. The Clinical Evaluation of Aureomycin.  
Brainerd, Henry, Lennette, Edwin H., Meiklejohn, Gordon,  
Bruyn, Henry B., Jr. and Clark, William H.  
Jour. Clin. Invest., 1949, 28 (5), 992-1005 (Sept.)
66. Q Fever. Method of O. C. Railsback, M.D., and Edwin H. Lennette, M.D.  
Railsback, O. C. and Lennette, Edwin H.  
Current Therapy, pp. 32-33. W. B. Saunders and Co.,  
Philadelphia, 1950.
67. La "Q Fever" dans la Californie du Nord.  
Lennette, Edwin H., Clark, William H. and Dean, Ben H.  
La Revue de Pathologie Comparee et d'Hygiene Generale, 1950,  
50, 426 (June)
68. Q Fever in California. I. Observations on Vaccination of Human  
Beings.  
Meiklejohn, Gordon and Lennette, Edwin H.  
Amer. Jour. Hyg., 1950, 52 (1), 54-64 (July)
69. Q Fever in California. II. Recovery of Coxiella burneti from  
Naturally-Infected Air-Borne Dust.  
DeLay, Paul D., Lennette, Edwin H. and DeOme, Kenneth B.  
Jour. Immunol., 1950, 65 (2), 211-220 (Aug.)
70. Symposium on Viral and Rickettsial Diseases. Part VI. 2. Newer  
Knowledge of the Older Rickettsial Diseases.  
Lennette, Edwin H.  
Bact. Rev., 1950, 14 (3), 249-258 (Sept.)
71. Immunity in Viral Diseases.  
Lennette, Edwin H.  
Cyclopedia of Medicine, Surgery and Specialities, Vol. 7,  
pp. 37-51. F. A. Davis Co., Philadelphia, 1950.

## 72. Q Fever (Queensland Fever; Balkan Grippe).

Lennette, Edwin H. and Clark, William H.

Nelson's Loose-leaf Medicine, Perpetual System of Living Medicine, Vol. I, Chapter V of Section on the Rickettsioses, pp. 883-895. Thomas Nelson and Sons, New York, 1950.

## 73. Observations on the Epidemiology of Q Fever in Northern California.

Lennette, Edwin H. and Clark, William H.

J.A.M.A., 1951, 145 (5), 306-309 (Feb. 3)

## 74. Q Fever in California. III. Aureomycin in the Therapy of Q Fever.

Clark, William H., Lennette, Edwin H. and Meiklejohn, Gordon

A.M.A. Arch. Int. Med., 1951, 87, 204-217 (Feb.)

## 75. Q Fever in California. V. Serologic Survey of Sheep, Goats and Cattle in Three Epidemiologic Categories, from Several Geographic Areas.

Lennette, Edwin H., Dean, Ben H., Abinanti, Francis R., Clark, William H., Winn, John F. and Holmes, Monroe A.

Amer. Jour. Hyg., 1951, 54 (1), 1-14 (July)

## 76. Q Fever in California. VI. Description of an Epidemic Occurring at Davis, California, in 1948.

Clark, William H., Bogucki, Alfred S., Lennette, Edwin H., Dean, Ben H. and Walker, John R.

Amer. Jour. Hyg., 1951, 54 (1), 15-24 (July)

## 77. Q Fever in California. VIII. An Epidemic of Q Fever in a Small Rural Community in Northern California.

Clark, William H., Romer, Mary S., Holmes, Monroe A., Welsh, Hartwell H., Lennette, Edwin H. and Abinanti, Francis R.

Amer. Jour. Hyg., 1951, 54 (1), 25-34 (July)

## 78. Q Fever in California. IX. An Outbreak Aboard a Ship Transporting Goats.

Clark, William H., Lennette, Edwin H. and Romer, Mary S.

Amer. Jour. Hyg., 1951, 54 (1), 35-43 (July)

79. Q Fever in California. X. Recovery of Coxiella burnetii from the Air of Premises Harboring Infected Goats.  
Lennette, Edwin H. and Welsh, Hartwell H.  
Amer. Jour. Hyg., 1951, 54 (1), 44-49 (July)
80. Western Equine and St. Louis Encephalitis in Man, California, 1945-1950.  
Lennette, Edwin H. and Longshore, W. Allen  
Calif. Med., 1951, 75 (3), 189-195 (Sept.)  
Also reprinted in California's Health, 1951, 9 (7), 49-53 (Oct. 15)  
and California's Health, 1951, 9 (8), 61-63 (Oct. 31)
81. Q Fever in California. VII. Clinical Features in One Hundred Eighty Cases.  
Clark, William H., Lennette, Edwin H., Railsback, Oscar C. and Romer, Mary S.  
A.M.A. Arch. Int. Med., 1951, 88, 155-167 (Aug.)
82. Q Fever. Method of O. C. Railsback, M.D., and Edwin H. Lennette, M.D.  
Railsback, O. C. and Lennette, Edwin H.  
Current Therapy, pp. 29-30. W. B. Saunders and Co., Philadelphia, 1951.
83. Interference Between Animal Viruses.  
Lennette, Edwin H.  
Annual Review of Microbiology, Vol. 5, pp. 277-294. George Banta Publishing Co., Stanford, 1951.
84. Q Fever in California. IV. Occurrence of Coxiella burnetii in the Placenta of Naturally Infected Sheep.  
Welsh, Hartwell H., Lennette, Edwin H., Abinanti, Francis R. and Winn, John F.  
Pub. Hlth. Rep., 1951, 66 (45), 1473-1477 (Nov. 9)
85. Q Fever in California. XI. An Epidemiologic Summary of 350 Cases Occurring in Northern California During 1948-1949.  
Clark, William H., Lennette, Edwin H. and Romer, Mary S.  
Amer. Jour. Hyg., 1951, 54 (3), 319-330 (Nov.)

Bibliography  
Edwin H. Lennette

86. Yellow Fever.

Lennette, Edwin H.

Cyclopedia of Medicine, Surgery and Specialties, Vol. 14,  
pp. 1027-1040. F. A. Davis Co., Philadelphia, 1951.

87. Q Fever Studies. XII. Certain Observations on the Relationships  
Between Serologic Tests for Brucellosis, Syphilis and Q Fever.

Lennette, Edwin H., Clark, William H. and Jensen, Florence W.

Amer. Jour. Pub. Hlth., 1952, 42 (1), 12-19 (Jan.)

88. Q Fever Studies. XIII. The Effect of Pasteurization on Coxiella  
burneti in Naturally Infected Milk.

Lennette, Edwin H., Clark, William H., Abinanti, Margery M.,  
Brunetti, Oscar and Covert, J. M.

Amer. Jour. Hyg., 1952, 55 (2), 246-253 (Mar.)

89. Q Fever Studies. XIV. Observations on the Pathogenesis of the  
Experimental Infection Induced in Sheep by the Intravenous Route.

Lennette, Edwin H., Holmes, Monroe A. and Abinanti, Francis R.

Amer. Jour. Hyg., 1952, 55 (2), 254-267 (Mar.)

90. Propagation of Dengue Virus Strains in Unweaned Mice.

Meiklejohn, Gordon, England, Beatrice and Lennette, Edwin H.

Amer. Jour. Trop. Med. and Hyg., 1952, 1 (1), 51-58 (Jan.)

91. Adaptation of Dengue Virus to the Hamster.

Meiklejohn, Gordon, England, Beatrice and Lennette, Edwin H.

Amer. Jour. Trop. Med. and Hyg., 1952, 1 (1), 59-65 (Jan.)

92. Evaluation of Monovalent Influenza Virus Vaccines. I. Observations  
on Antibody Response Following Vaccination.

Meiklejohn, Gordon, Weiss, Daniel L., Shragg, Robert I. and  
Lennette, Edwin H.

Amer. Jour. Hyg., 1952, 55 (1), 1-11 (Jan.)

## Bibliography

Edwin H. Lennette

93. Evaluation of Monovalent Influenza Vaccines. II. Observations During an Influenza A-Prime Epidemic.  
 Meiklejohn, Gordon, Kempe, C. H., Thalman, W. G. and Lennette, Edwin H.  
 Amer. Jour. Hyg., 1952, 55 (1), 12-21 (Jan.)
94. Q Fever Studies. XV. Development and Persistence in Man of Complement-Fixing and Agglutinating Antibodies to Coxiella burnetii.  
 Lennette, Edwin H., Clark, William H., Jensen, Florence W. and Toomb, Carolyn J.  
 Jour. Immunol., 1952, 68 (5), 591-598 (May)
95. Culture Collections of Microorganisms.  
 Raper, Kenneth B., Buchanan, R. E., Burkholder, F. R., Cleland, R. E., Coghill, R. D., Enders, John F., Lamanna, Carl, Lennette, E. H., McKinney, H. H., Robbins, Wm. J. and Warren, Joel  
 Science, 1952, 116 (3007), 179-180 (Aug. 15)
96. Treatment of Q Fever with Antibiotics.  
 Clark, William H. and Lennette, Edwin H.  
 Ann. N.Y. Acad. Sci., 1952, 55 (Art. 6), 1004-1018 (Dec.)
97. Virus Diseases and the Public Health.  
 Merrill, Malcolm H. and Lennette, Edwin H.  
 California's Health, 1953, 10 (14), 105-109 (Jan. 31)
98. World Distribution of Q Fever: Human, Animal and Arthropod Infection.  
 Berge, T. O. and Lennette, Edwin H.  
 Amer. Jour. Hyg., 1953, 57 (2), 125-143 (Mar.)
99. Q Fever: A Study of Serological Relationships Among Strains of Coxiella burnetii (Derrick).  
 Berge, T. O. and Lennette, Edwin H.  
 Amer. Jour. Hyg., 1953, 57 (2), 144-169 (Mar.)

Bibliography  
Edwin H. Lennette

-15-

100. Q Fever Studies. XVI. Some Aspects of the Experimental Infection Induced in Sheep by the Intratracheal Route of Inoculation.
- Abinanti, Francis R., Welsh, Hartwell H., Lennette, Edwin H. and Brunetti, Oscar.
- Amer. Jour. Hyg., 1953, 57 (2), 170-184 (Mar.)
101. The 1952 Outbreak of Encephalitis in California. Laboratory Methods for Etiologic Diagnosis.
- Lennette, Edwin H., Nyberg, Marjorie C., Barghausen, Dolores M., Chin, Roland, Fujimoto, Frances Y. and Itatani, Margaret K.
- Calif. Med., 1953, 79 (2), 78-83 (Aug.)
102. Q Fever Studies. XVII. Presence of Coxiella burnetii in the Feces of Naturally Infected Sheep.
- Winn, John F., Lennette, Edwin H., Welsh, Hartwell H. and Abinanti, Francis R.
- Amer. Jour. Hyg., 1953, 58 (2), 183-187 (Sept.)
103. Q Fever: A Summary of One Year's (1948) Observations in Central and Northern California.
- Lennette, E. H., Clark, W. H. and Dean, B. H.
- Proc. Seventh Pacific Sci. Congress, 1953, 7, 334-340
104. Q Fever Studies. XVIII. Presence of Coxiella burnetii in the Birth Fluids of Naturally Infected Sheep.
- Abinanti, Francis R., Lennette, Edwin H., Winn, John F. and Welsh, Hartwell H.
- Amer. Jour. Hyg., 1953, 58 (3), 385-388 (Nov.)
105. Western Equine Encephalitis in Infants. A Report on Three Cases with Sequelae.
- Bruyn, Henry B. and Lennette, Edwin H.
- Calif. Med., 1953, 79 (5), 362-366 (Nov.)

## Bibliography

Edwin H. Lennette

106. An Evaluation of Diagnostic Procedures for Virus and Rickettsial Diseases.

Lennette, Edwin H.

The Dynamics of Virus and Rickettsial Infections, pp. 348-371.  
The Blakiston Co., Inc., New York, 1954.

107. Chemotherapy of Primary Atypical Pneumonia.

Meiklejohn, Gordon, Thalman, William G., Waligora, Daniel J.,  
Kempe, C. Henry and Lennette, Edwin H.

J.A.M.A., 1954, 154, 553-557 (Feb. 13)

108. Immunity in Viral Diseases.

Lennette, Edwin H.

Cyclopedia of Medicine, Surgery and Specialties, Vol. 7,  
pp. 37-52G. F. A. Davis Co., Philadelphia, 1954.

109. Effectiveness of Polyvalent Influenza A Vaccine During an Influenza A-Prime Epidemic.

Meiklejohn, Gordon, Kempe, C. Henry, Thalman, William G.  
and Lennette, Edwin H.

Amer. Jour. Hyg., 1954, 59 (3), 241-248 (May)

110. Experimental Observations on a Skin-Test Antigen for Western Equine Encephalomyelitis.

Shinefield, Henry R., Lennette, Edwin H. and Longshore,  
W. Allen, Jr.

Jour. Immunol., 1955, 74 (3), 179-187 (Mar.)

111. Q Fever Studies. XIX. Presence and Epidemiologic Significance of Coxiella burnetii in Sheep Wool.

Abinanti, Francis R., Welsh, Hartwell H., Winn, John F.  
and Lennette, Edwin H.

Amer. Jour. Hyg., 1955, 61 (3), 362-370 (May)

Bibliography  
Edwin H. Lennette

112. A Complement Fixation Test for Poliomyelitis.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Exper. Med., 1955, 102 (2), 133-150 (Aug.1)
113. Studies on a Complement Fixation Test for Herpes Simplex.  
Sosa-Martinez, Jose and Lennette, Edwin H.  
Jour. Bact., 1955, 70 (2), 205-215 (Aug.)
114. Studies on a Skin Test for Western Equine Encephalitis. Preliminary Evaluation in Man.  
Shinefield, Henry R., Longshore, W. Allen, Jr. and Lennette, Edwin H.  
Jour. Immunol., 1955, 75 (3), 227-238 (Sept.)
115. Etiology of Acute Respiratory Disease Among Service Personnel at Fort Ord, California.  
Berge, T. O., England, Beatrice, Mauris, Carmen, Shuey, Harold E. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1955, 62 (3), 283-294 (Nov.)
116. Etiologic Aspects of the Infectious Encephalitides.  
Lennette, Edwin H.  
Proc. and Papers, Calif. Mosquito Control Assn., 23rd Annual Conference, and 11th Annual Meeting, Amer. Mosquito Control Assn. (Issued Dec. 7, 1955)
117. Epidemiologic Observations on Acute Infectious Encephalitis in California, with Special Reference to the 1952 Outbreak.  
Longshore, W. Allen, Jr., Stevens, Ida May, Hollister, Arthur C., Jr., Gittelsohn, Alan and Lennette, Edwin H.  
Amer. Jour. Hyg., 1956, 63 (1), 69-86 (Jan.)
118. Serological Response to Japanese B Encephalitis Vaccine of Children and Horses Immune to St. Louis Virus.  
Hammon, W. McD., Sather, Gladys E., Lennette, Edwin H. and Reeves, W. C.  
Proc. Soc. Exper. Biol. and Med., 1956, 91 (3), 517-521 (Mar.)

## Bibliography

Edwin H. Lennette

119. Symposium on Newer Knowledge of Viral and Rickettsial Diseases. Introduction. (Papers presented at Annual Meeting of the American Society of Tropical Medicine and Hygiene, Boston, Massachusetts, November 3, 1955)

Lennette, Edwin H.

Amer. Jour. Trop. Med. and Hyg., 1956, 5 (3), 419-421 (May)

120. Modification of the Homotypic Specificity of Poliomyelitis Complement-Fixing Antigens by Heat.

Schmidt, Nathalie J. and Lennette, Edwin H.

Jour. Exper. Med., 1956, 104 (1), 99-120 (July)

121. Q Fever.

Lennette, Edwin H.

Meakins' Practice of Medicine, Sixth Edition, Chapter 64, pp. 469-473. The C. V. Mosby Co., St. Louis, 1956.

122. General Principles Underlying Laboratory Diagnosis of Virus and Rickettsial Infections.

Lennette, Edwin H.

Diagnostic Procedures for Virus and Rickettsial Diseases, Second Edition, Chapter 1, pp. 1-52. American Public Health Assn., New York, 1956.

123. A Chick Embryo-Derived Complement-Fixing Antigen for Western Equine Encephalomyelitis.

Lennette, Edwin H., Wiener, Anna, Weff, Beverly Jean and Hoffman, Marjorie N.

Proc. Soc. Exper. Biol. and Med., 1956, 92 (3), 575-577 (July)

124. Rapid Identification of Isolates of Western Equine Encephalomyelitis Virus by the Complement-Fixation Technique.

Lennette, Edwin H., Wiener, Anna, Ota, Margaret I., Fujimoto, Frances Y. and Hoffman, Marjorie N.

Amer. Jour. Hyg., 1956, 64 (3), 270-275 (Nov.)

Bibliography  
Edwin H. Lennette

125. Isolation of Western Equine Encephalomyelitis Virus from Naturally-Infected Squirrels in California.  
Lennette, Edwin H., Ota, Margaret I., Dobbs, Martha E. and Browne, Alcor S.  
Amer. Jour. Hyg., 1956, 64 (3), 276-280 (Nov.)
126. A Colorimetric Method for the Typing of Adenoviruses.  
Lennette, Edwin H., Neff, Beverly Jean and Fox, Virginia L.  
Amer. Jour. Hyg., 1957, 65 (1), 94-109 (Jan.)
127. Studies on the Development and Persistence of Complement-Fixing and Neutralizing Antibodies in Human Poliomyelitis.  
Lennette, Edwin H. and Schmidt, Nathalie J.  
Amer. Jour. Hyg., 1957, 65 (2), 210-238 (Mar.)
128. Laboratory Diagnosis of Herpetic Infections of the Eye.  
Lennette, Edwin H. and van Allen, Alwine  
Amer. Jour. Ophthalmology, 1957, 43 (4), Part II, 118-126 (Apr.)
129. Factors Influencing the Potency of Poliomyelitis Complement-Fixing Antigens Produced in Tissue-Culture Systems.  
Schmidt, Nathalie J., Lennette, Edwin H., Doleman, Jessie H. and Hagens, Shirley J.  
Amer. Jour. Hyg., 1957, 66 (1), 1-19 (July)
130. An Inquiry into the Use of the Complement-Fixation Test for the Typing of Poliomyelitis Viruses.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1957, 66 (2), 119-130 (Sept.)
131. Immunologic Factors in Viral Infections. With Comments on Their Bearing on Certain Cancer Problems.  
Lennette, Edwin H.  
Texas Reports on Biol. and Med., 1957, 15 (3), 477-495 (Fall)

## Bibliography

Edwin H. Lennette

132. Turlock Virus: A Presumably New Arthropod-Borne Virus. Isolation and Identification.  
Lennette, Edwin H., Ota, Margaret I., Fujimoto, Frances Y., Wiener, Anna and Loomis, Edmond C.  
Amer. Jour. Trop. Med. and Hyg., 1957, 6 (6), 1024-1035 (Nov.)
133. Turlock Virus: A Description of Some of its Properties.  
Lennette, Edwin H., Ota, Margaret I. and Hoffman, Marjorie N.  
Amer. Jour. Trop. Med. and Hyg., 1957, 6 (6), 1036-1046 (Nov.)
134. Vaccination Against Asian Influenza. Basis for Recommendations and a Preliminary Report on Efficacy.  
Commission on Influenza\*  
J.A.M.A., 1957, 165 (16), 2055-2058 (Dec. 21)
135. The Protective Effect of Monovalent Asian-Strain Vaccine Against Asian Influenza.  
Culver, James O., Nitz, Robert E. and Lennette, Edwin H.  
J.A.M.A., 1957, 165 (17), 2174-2177 (Dec. 28)
136. Arthropod-Borne Viral Encephalitides. Epidemiology of Western Equine and St. Louis Encephalitis.  
Lennette, Edwin H.  
Viral Encephalitis. A Symposium, Fifth Annual Scientific Meeting of the Houston Neurological Society, Texas Medical Center, Houston, Texas, Fields, William S. and Blattner, Russell J., Eds., pp. 22-42. Charles C. Thomas. Springfield. 1958.
137. Isolation and Identification of Western Equine Encephalomyelitis Virus from Mosquitoes by Tissue Culture Methods.  
Welsh, Hartwell H., Neff, Beverly Jean and Lennette, Edwin H.  
Amer. Jour. Trop. Med. and Hyg., 1958, 7 (2), 187-196 (Mar.)

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## Bibliography

Edwin H. Lennette

138. Acute Benign Pericarditis. Report of Two Cases Associated with Group A and Group B Coxsackie Viruses.

Movitt, Eli R., Lennette, Edwin H., Mangum, Jack F., Berk, Morris and Bowman, Murdock S.

New Eng. Jour. Med., 1958, 258, 1082-1086 (May 29)

139. A Colorimetric Method for the Typing of Coxsackie Viruses of Group B and Certain Members of Group A.

Schmidt, Nathalie J., Midulla, Mario and Lennette, Edwin H.

Jour. Immunol., 1958, 80 (6), 454-462 (June)

140. Viral Infections of the Upper Respiratory Tract.

Lennette, Edwin H.

Trans. Amer. Acad. Ophthalmology and Otolaryngology, 1958, Section on Symposium: Viruses and Viral Diseases, pp. 399-410 (May-June)

141. Air-Borne Transmission of Q Fever: The Role of Parturition in the Generation of Infective Aerosols.

Welsh, Hartwell H., Lennette, Edwin H., Abinanti, Francis R. and Winn, John F.

Ann. N.Y. Acad. Sci., 1958, 70 (Art. 3), 528-540 (June 3)

142. The Isolation and Identification of Turlock Virus in Tissue Culture.

Welsh, Hartwell H., Neff, Beverly Jean and Lennette, Edwin H.

Amer. Jour. Trop. Med. and Hyg., 1958, 7 (5), 536-542 (Sept.)

143. The Type-Specific Reactivity of the Influenza Complement Fixation Test. Inability of Allantoic Fluid Antigens to Distinguish Between Asian and Other Recent Type A Influenza Virus Infections.

Lennette, Edwin H., Culver, James O. and Stevens, Thirza E.

Jour. Lab. and Clin. Med., 1958, 52 (4), 605-611 (Oct.)

## Bibliography

Edwin H. Lennette

144. The Behavior of Different Strains of Poliomyelitis Virus in the Complement Fixation Reaction. I. Comparison of Sensitivity of Antigens Derived from Laboratory Strains and Patient's Own Infecting Strain.
- Schmidt, Nathalie J. and Lennette, Edwin H.
- Jour. Immunol., 1958, 81 (4), 309-316 (Oct.)
145. Problems of the Viral Diagnostic Laboratory with Respect to Poliomyelitis.
- Lennette, Edwin H.
- Poliomyelitis. Papers and Discussions Presented at the Fourth International Poliomyelitis Conference, pp. 377-386. J. B. Lippincott Co., Philadelphia, 1958.
146. The Recall Phenomenon in the Antibody Response to Influenza Vaccines.
- Culver, James O., Lennette, Edwin H., Navarre, George and Donahue, Gwendolyn A.
- Jour. Immunol., 1958, 81 (6), 452-459 (Dec.)
147. The Coe Virus. An Apparently New Virus Recovered from Patients with Mild Respiratory Disease.
- Lennette, Edwin H., Fox, Virginia L., Schmidt, Nathalie J. and Culver, James O.
- Amer. Jour. Hyg., 1958, 68 (3), 272-287 (Nov.)
148. The Varied Clinical Manifestations of Coxsackie Virus Infections. Observations and Comments on an Outbreak in California.
- Gordon, Robert B., Lennette, Edwin H. and Sandrock, Rachel S.
- A.M.A. Arch. Int. Med., 1959, 103 (1), 63-75 (Jan.)
149. Q Fever.
- Lennette, Edwin H.
- Viral and Rickettsial Infections of man, Third Edition, Chapter 45, pp. 880-895. J. B. Lippincott Co., Philadelphia, 1959.

Bibliography  
Edwin H. Lennette

150. Serologic Reactions in Viral and Rickettsial Infections.  
Lennette, Edwin H.  
Viral and Rickettsial Infections of Man, Third Edition,  
Chapter 10, pp. 230-250. J. B. Lippincott Co., Philadelphia, 1959.
151. Psittacosis (Ornithosis). Method of Edwin H. Lennette, M.D., Ph.D.  
Lennette, Edwin H.  
Current Therapy, Eleventh Edition, page 34. W. B. Saunders  
Co., Philadelphia, 1959.
152. Naturally Acquired Toxoplasmosis in the Gray Squirrel, Sciurus  
griseus, and its Bearing on the Laboratory Diagnosis of Rabies.  
Soave, Orland A. and Lennette, Edwin H.  
Jour. Lab. and Clin. Med., 1959, 53 (1), 163-166 (Jan.)
153. A Long-Term Study of Antibody Response to an Adenovirus Vaccine and  
Observations on the Effect of Concurrent Adenovirus Disease.  
Culver, James O., Lennette, Edwin H., Fox, Virginia L. and  
Flintjer, John D.  
Amer. Jour. Hyg., 1959, 69 (1), 38-48 (Jan.)
154. Spontaneous Disappearance of the Slow-Sedimenting Components  
of Influenza Virus Preparations.  
Frommhagen, Laurence H. and Lennette, Edwin H.  
Virology, 1959, 7 (2), 247-248 (Feb.)
155. Adenovirus Vaccine. A Study of the Complement-Fixing and Neutralizing  
Antibody Response.  
Culver, James O., Lennette, Edwin H., Flintjer, John D.,  
Stevens, Thirza E. and Fox, Virginia L.  
Amer. Jour. Hyg., 1959, 69 (2), 112-119 (Mar.)
156. Adenovirus Vaccine. A Field Evaluation of Protective Capacity Against  
Respiratory Disease.  
Culver, James O., Lennette, Edwin H. and Flintjer, John D.  
Amer. Jour. Hyg., 1959, 69 (2), 120-126 (Mar.)

Bibliography  
Edwin H. Lennette

157. The Laboratory Diagnosis of Viral Disease.  
Lennette, Edwin H.  
Kaiser Foundation Med. Bull., 1959, 7 (1), 12-24 (Jan.-Mar.)
158. Serologic Reactions in Adenovirus Disease. I. Delayed Complement-Fixing Antibody Response.  
Culver, James O., Lennette, Edwin H. and Green, Lucile  
Jour. Lab. and Clin. Med., 1959, 53 (2), 241-246 (Feb.)
159. Epidemiologic Observations of an Outbreak of Asian-Strain Influenza in a Closed Population.  
Stallones, Reuel A. and Lennette, Edwin H.  
Amer. Jour. Pub. Hlth., 1959, 49 (5), 656-667 (May)
160. Immunological Evaluation of Monovalent Influenza Vaccine in Adults and in Children.  
Bruyn, Henry B. and Lennette, Edwin H.  
A.M.A. Arch. Int. Med., 1959, 103 (6), 914-923 (June)
161. Transplacental Passage of Antibody to Western Equine and St. Louis Encephalitis Viruses.  
Longshore, William Allen, Jr., Ota, Margaret I., Hoffman, Marjorie N., Fujimoto, Frances Y. and Lennette, Edwin H.  
Amer. Jour. Trop. Med. and Hyg., 1959, 8 (4), 424-432 (July)
162. A Microflocculation Test for Poliomyelitis. With Observations on the Flocculating Antibody Response in Human Poliomyelitis.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1959, 70 (1), 51-65 (July)
163. Q Fever Studies. XX. Comparison of Four Serologic Techniques for the Detection and Measurement of Antibody to Coxiella burnetii in Naturally Exposed Sheep.  
Welsh, Hartwell H., Jensen, Florence W. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1959, 70 (1), 1-13 (July)

## Bibliography

Edwin H. Lennette

164. Q Fever Studies. XXI. The Recovery of Coxiella burnetii from the Soil and Surface Water of Premises Harboring Infected Sheep.
- Welsh, Hartwell H., Lennette, Edwin H., Abinanti, Francis R., Winn, John F. and Kaplan, William
- Amer. Jour. Hyg., 1959, 70 (1), 14-20 (July)
165. Comparison of the Sensitivity of Several Mammalian Cell Types for the Isolation of Poliomyelitis Viruses from Man.
- Chadwick, David L., Welsh, Hartwell H. and Lennette, Edwin H.
- Jour. Lab. and Clin. Med., 1959, 54 (3), 409-416 (Sept.)
166. Viral Disease of the Central Nervous System. Influence of Poliomyelitis Vaccination on Etiology.
- Lennette, Edwin H., Magoffin, Robert L., Schmidt, Nathalie J. and Hollister, Arthur C., Jr.
- J.A.M.A., 1959, 171 (11), 1456-1464 (Nov. 14)
167. Epidemiology of Q Fever.
- Lennette, Edwin H.
- Arch. de l'Institut Pasteur de Tunis, 1959, 36 (3-4), 521-527 (Dec.)
168. The Epidemiology of Q Fever.
- Lennette, Edwin H.
- Proc. Sixth Int. Cong. on Trop. Med. and Malaria, Lisbon, Portugal, Sept. 5-13, 1958, Vol. 5, pp. 703-710, 1959.
169. Psittacosis (Ornithosis). Method of Edwin H. Lennette, M.D., Ph.D.
- Lennette, Edwin H.
- Current Therapy, Twelfth Edition, pp. 38-39. W. B. Saunders Co., Philadelphia, 1960.

Bibliography  
Edwin H. Lennette

170. The Response to Influenza Vaccines as Determined by Levels of Complement-Fixing Antibody in the Acute-Phase Sera of Patients with Respiratory Disease.

Culver, James O., Lennette, Edwin H., Navarre, George and Kempe, C. Henry

Jour. Immunol., 1960, 84 (1), 98-105 (Jan.)

171. The Behavior of Different Strains of Poliomyelitis Virus in the Complement Fixation Reaction. II. The Sensitivity and Specificity of Antigens Derived from Various Strains.

Schmidt, Nathalie J., Lennette, Edwin H., Hagens, Shirley J. and Dennis, Juanita

Jour. Immunol., 1960, 84 (2), 160-170 (Feb.)

172. A Fatal Human Case of Rabies Following the Bite of a Rabid Bat (Lasionycteris noctivagans). Isolation and Identification of the Virus from Vector and Victim.

Lennette, Edwin H., Soave, Orland A., Nakamura, Koichi and Kellogg, Grandon H., Jr.

Jour. Lab. and Clin. Med., 1960, 55 (1), 89-93 (Jan.)

173. Adenovirus Vaccine: Evaluation of Antibody Response and Protective Efficacy and Comparison with an Earlier Preparation.

Lennette, Edwin H., Flintjer, John D., Culver, James O., Fox, Virginia L. and Stevens, Thirza E.

Amer. Jour. Hyg., 1960, 71 (2), 193-203 (Mar.)

174. Mumps Virus Infection Simulating Paralytic Poliomyelitis. A Report of 11 Cases.

Lennette, Edwin H., Caplan, Gerald E. and Magoffin, Robert L.

Pediatrics, 1960, 25 (5), Part I, 788-797 (May)

175. Sobre un Antigeno Soluble del Virus del Herpes Simple.

Sosa-Martínez, José and Lennette, Edwin H.

Ciencia (Mex.), 1960, 19 (11-12), 249-258 (Apr. 25)

Bibliography  
Edwin H. Lennette

176. California Encephalitis Surveillance Program. Mosquito-Virus Relationships.
- Meyers, Ernest G., Loomis, Edmond C., Fujimoto, Frances Y., Ota, Margaret I. and Lennette, Edwin H.
- Amer. Jour. Hyg., 1960, 71 (3), 368-377 (May)
177. California Encephalitis Surveillance Program. Relationship of Human Morbidity and Virus Isolation from Mosquitoes.
- Longshore, W. Allen, Jr., Lennette, Edwin H., Peters, Richard F., Loomis, Edmond C. and Meyers, Ernest G.
- Amer. Jour. Hyg., 1960, 71 (3), 389-400 (May)
178. The Behavior of Different Strains of Poliomyelitis Virus in the Complement Fixation Reaction. III. Comparison of the Potency of Complement Fixing Antigens Derived from Different Strains of Poliomyelitis Virus.
- Schmidt, Nathalie J., Lennette, Edwin H., Dennis, Juanita and Hagens, Shirley J.
- Jour. Immunol., 1960, 85 (1), 67-71 (July)
179. Indolent, or So-Called Serous Otitis Media. Including Combined Allergy and Virus Studies.
- Fishman, Louis Z., Lennette, Edwin H. and Dannenberg, Thurman B.
- A.M.A. Arch. Otolaryngology, 1960, 72 (1), 25-30 (July)
180. A Complement-Fixing Antigen for Herpes Simplex Derived from Chick-Embryo Tissue Cultures.
- Schmidt, Nathalie J., Lennette, Edwin H. and Shon, Carol W.
- Amer. Jour. Hyg., 1960, 72 (1), 59-72 (July)
181. Evaluation of an Adenovirus Vaccine in a Dispensary Population.
- Stallones, Reuel A., Lennette, Edwin H., Nitz, Robert E. and Holguin, Alfonso H.
- Amer. Jour. Hyg., 1960, 72 (1), 100-110 (July)

Bibliography  
Edwin H. Lennette

182. Antibody Response to Influenza Vaccines Containing the Asian Strain.  
Culver, James O., Lennette, Edwin H., Stevens, Thirza E.  
and Nitz, Robert E.  
Jour. Immunol., 1960, 85 (2), 197-202 (Aug.)
183. Q Fever.  
Lennette, Edwin H.  
Encyclopaedia Britannica, Inc., Vol. 18, page 808. William  
Benton, Chicago, 1960.
184. Infectious Canine Hepatitis Coincidentally Associated with  
Vaccination Against Rabies.  
Soave, Orland A. and Lennette, Edwin H.  
Amer. Jour. Pub. Hlth., 1960, 50 (10), 1582-1587 (Oct.)
185. An Etiologic Study of Clinical Paralytic Poliomyelitis.  
Magoffin, Robert L., Lennette, Edwin H., Hollister, Arthur C.,  
Jr. and Schmidt, Nathalie J.  
J.A.M.A., 1961, 175 (4), 269-278 (Jan. 28)
186. Vesicular Stomatitis and Exanthem. A Syndrome Associated with  
Coxsackie Virus, Type A16.  
Magoffin, Robert L., Jackson, Edwin W. and Lennette, Edwin H.  
J.A.M.A., 1961, 175 (6), 441-445 (Feb. 11)
187. Q Fever Studies. XXII. Inoculation of Sheep by the Intestinal  
Route.  
Winn, John F., Abinanti, Francis R., Lennette, Edwin H.  
and Welsh, Hartwell H.  
Amer. Jour. Hyg., 1961, 73 (1), 105-113 (Jan.)
188. A Colorimetric Neutralization Test for Herpes Simplex, with  
Observations on Neutralizing and Complement-Fixing Antibody  
Levels in Human Sera.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Immunol., 1961, 86 (2), 137-145 (Feb.)

Bibliography  
Edwin H. Lennette

189. Laboratory Diagnosis of Influenza by Virus Isolation.  
Lennette, Edwin H.  
Amer. Rev. Resp. Dis., 1961, 83 (2), 116-119 (Feb.)
190. Observations on the Neutralizing Antibody Response to Group B  
Coxsackie Viruses in Patients with Central Nervous System Disease.  
Lennette, Edwin H., Shinomoto, Tak T., Schmidt, Nathalie J.  
and Magoffin, Robert L.  
Jour. Immunol., 1961, 86 (3), 257-266 (Mar.)
191. Recent Advances in the Serodiagnosis of Virus Infections.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Progress in Medical Virology, Vol. 3, pp. 1-58. Karger,  
Basel/New York, 1961.
192. Application of Tissue Culture Technics to Diagnostic Virology  
in the Public Health Laboratory.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Pub. Hlth., 1961, 51 (4), 511-516 (Apr.)
193. Observations on the Complement-Fixing Antibody Response to Polio-  
virus in Patients with Certain Coxsackie and ECHO Virus Infections.  
Lennette, Edwin H., Schmidt, Nathalie J. and Magoffin, Robert L.  
Jour. Immunol., 1961, 86 (5), 552-560 (May)
194. Immunologic Identification of Coxsackie A21 Virus with Coe Virus.  
Schmidt, Nathalie J., Fox, Virginia L. and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1961, 107 (1), 63-65 (May)
195. Association of Coxsackie Viruses with Illnesses Resembling Mild  
Paralytic Poliomyelitis.  
Magoffin, Robert L., Lennette, Edwin H. and Schmidt, Nathalie J.  
Pediatrics, 1961, 28 (4), 602-613 (Oct.)

Bibliography  
Edwin H. Lennette

196. A Comparative Study of Monkey Kidney Cell Cultures and Suckling Mice for the Recovery of Enteroviruses from Patients with Central Nervous System Disease.
- Lennette, Edwin H., Wiener, Anna, Hoshiwara, Isao, Woodie, James and Magoffin, Robert L.
- Jour. Lab. and Clin. Med., 1961, 58 (4), 634-643 (Oct.)
197. Pattern of Respiratory Virus Infections in Army Recruits.
- Lennette, Edwin H., Stallones, Reuel A. and Holguin, Alfonso H.
- Amer. Jour. Hyg., 1961, 74 (3), 225-233 (Nov.)
198. Typing of ECHO Virus Isolates by Immune Serum Pools. The "Intersecting Serum Scheme".
- Schmidt, Nathalie J., Guenther, Raymond W. and Lennette, Edwin H.
- Jour. Immunol., 1961, 87 (5), 623-626 (Nov.)
199. Comparative Sensitivity of Four Host Systems for the Isolation of Certain Arthropod-Borne Viruses from Mosquitoes.
- Lennette, Edwin H., Ota, Margaret I., Ho, Helen and Schmidt, Nathalie J.
- Amer. Jour. Trop. Med. and Hyg., 1961, 10 (6), 897-904 (Nov.)
200. An Etiologic Study of Seasonal Aseptic Meningitis and Encephalitis in the Central Valley of California.
- Lennette, Edwin H., Magoffin, Robert L., Longshore, W. Allen, Jr. and Hollister, Arthur C., Jr.
- Amer. Jour. Trop. Med. and Hyg., 1961, 10 (6), 885-896 (Nov.)
201. Complement-Fixing Antibody Response to Inactivated Poliovirus Vaccine.
- Lennette, Edwin H., Schmidt, Nathalie J. and Magoffin, Robert L.
- Jour. Immunol., 1961, 87 (6), 696-706 (Dec.)
202. Viral Central Nervous System Disease. An Etiologic Study Conducted at the Los Angeles County General Hospital.
- Lennette, Edwin H., Magoffin, Robert L. and Knouf, Evelynne G.
- J.A.M.A., 1962, 179 (9), 687-695 (Mar. 3)

Bibliography  
Edwin H. Lennette

203. Studies on Hemagglutination and Hemagglutination-Inhibition Tests for Identification of ECHO Viruses.  
Schmidt, Nathalie J., Dennis, Juanita, Hagens, Shirley J. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1962, 75 (1), 74-85 (Jan.)
204. Studies on the Antibody Responses of Patients Infected with ECHO Viruses.  
Schmidt, Nathalie J., Dennis, Juanita, Hagens, Shirley J. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1962, 75 (2), 168-182 (Mar.)
205. Colorimetric Test in HeLa Cell System for Assay of Neutralizing Antibodies to ECHO Viruses.  
Schmidt, Nathalie J., Shinomoto, Tak T., Dennis, Juanita, Hagens, Shirley J., Fox, Virginia L. and Lennette, Edwin H.  
Jour. Lab. and Clin. Med., 1962, 59 (4), 687-696 (Apr.)
206. Q Fever Studies. XXIII. Antibody Patterns Against Coxiella burnetii.  
Lackman, David B., Frommshagen, Laurence H., Jensen, Florence W. and Lennette, Edwin H.  
Amer. Jour. Hyg., 1962, 75 (2), 158-167 (Mar.)
207. Complement-Fixing Antibody Responses to ECHO Virus Types 12 and 19 of Patients with Enterovirus Infections.  
Schmidt, Nathalie J., Dennis, Jaunita and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1962, 109 (2), 364-369 (Feb.)
208. Recovery of a Newly Recognized Enterovirus from Patients with Aseptic Meningitis.  
Lennette, Edwin H., Schmidt, Nathalie J., Magoffin, Robert L. and Wiener, Anna  
New Eng. Jour. Med., 1962, 266 (26), 1358-1361 (June 28)

Bibliography  
Edwin H. Lennette

209. Nonpolioviruses and Paralytic Disease.  
Magoffin, Robert L. and Lennette, Edwin H.  
Calif. Med., 1962, 97 (1), 1-7 (July)
210. Gel Double Diffusion Studies with Group B and Group A, Type 9  
Coxsackie Viruses. I. The Technique and Reactions Obtained  
with Hyperimmune Animal Sera and Human Sera.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Immunol., 1962, 89 (1), 85-95 (July)
211. Gel Double Diffusion Studies with Group B and Group A, Type 9  
Coxsackie Viruses. II. Serologic Diagnosis of Coxsackie Virus  
Infections by the Gel Double Diffusion Technique.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Immunol., 1962, 89 (1), 96-105 (July)
212. A Simplified Immunofluorescent Plaque Method.  
Spendlove, Rex S. and Lennette, Edwin H.  
Jour. Immunol., 1962, 89 (1), 106-112 (July)
213. The Price Virus. An Unclassified Enterovirus Isolated From  
Patients with Central Nervous System Disease.  
Lennette, Edwin H., Schmidt, Nathalie J., Magoffin, Robert L.,  
Dennis, Juanita and Wiener, Anna  
Proc. Soc. Exper. Biol. and Med., 1962, 110 (4), 769-775  
(Aug.-Sept.)
214. Observations on the Complement-Fixing Antibody Response in Human  
Poliomyelitis. Influence of Age and Vaccination Status.  
Lennette, Edwin H., Magoffin, Robert L. and Schmidt,  
Nathalie J.  
Jour. Immunol., 1962, 89 (3), 358-366 (Sept.)
215. The Prophylactic Efficacy of Adenovirus Vaccines.  
Lennette, Edwin H.  
Jour. Hyg., Epidemiol., Microbiol. and Immunol., Prague,  
1962, 6 (3), 334-338

Bibliography  
Edwin H. Lennette

216. Oral Poliovirus Vaccine.  
Lennette, Edwin H. and Magoffin, Robert L.  
California's Health, 1962, 20 (9), 68-69 (Nov. 1)
217. Controlling Viral Diseases of the Central Nervous System.  
Lennette, Edwin H.  
Quarterly Bull. Wisconsin State Board of Health, 1962, 15 (5),  
23-24 and 30 (Apr., May, June)
218. Studies on the Hemagglutination of Coe (Coxsackie A21) Virus.  
Schmidt, Nathalie J., Fox, Virginia L. and Lennette,  
Edwin H.  
Jour. Immunol., 1962, 89 (5), 672-683 (Nov.)
219. Fatal Infection in an Infant Associated with Coxsackie Virus  
Group A, Type 16.  
Wright, Harry T., Jr., Landing, Benjamin H., Lennette, Edwin H.  
and McAllister, Robert M.  
New Eng. Jour. Med., 1963, 268 (19), 1041-1044 (May 9)
220. Development of Viral Antigen and Infectious Virus in HeLa Cells  
Infected with Reovirus.  
Spendlove, Rex S., Lennette, Edwin H., Knight, Charles O. and  
Chin, Jean N.  
Jour. Immunol., 1963, 90 (4), 548-553 (Apr.)
221. The Role of the Mitotic Apparatus in the Intracellular Location of  
Reovirus Antigen.  
Spendlove, Rex S., Lennette, Edwin H. and John, A. Charlotte  
Jour. Immunol., 1963, 90 (4), 554-560 (Apr.)
222. Serologic Reactivity of Certain Antigens Obtained by Fractionation  
of Coxsackie Viruses in Cesium Chloride Density Gradients.  
Schmidt, Nathalie J., Dennis, Juanita, Frommshagen, Laurence H.  
and Lennette, Edwin H.  
Jour. Immunol., 1963, 90 (4), 654-662 (Apr.)

Bibliography  
Edwin H. Lennette

223. Serologic Responses to Para-Influenza Viruses in Patients with Mumps Virus Infection.
- Lennette, Edwin H., Jensen, Florence W., Guenther, Raymond W. and Magoffin, Robert L.
- Jour. Lab. and Clin. Med., 1963, 61 (5), 780-788 (May)
224. The Value of Military Populations for Studies of Viral Respiratory Disease.
- Stallones, Reuel A. and Lennette, Edwin H.
- Amer. Rev. Resp. Dis., 1963, 88 (3) Part 2, 89-93 (Sept.)
225. Comparative Sensitivity of Two Inoculation Technics for Isolation of Viruses from Stool Specimens.
- Schmidt, Nathalie J., Ho, Helen H., King, Carole J. and Lennette, Edwin H.
- Amer. Jour. Clin. Path., 1964, 41 (2), 227-229 (Feb.)  
Also reprinted in Tech. Bull. Reg. Med. Technol., 1964, 34 (1), 11-13 (Jan.)
226. A Comparison of the Reactivity of Poliovirus Complement-Fixing Antigens (Native, Heated and Sucrose Density Gradient C and D) with Human Sera.
- Lennette, Edwin H., Schmidt, Nathalie J., Magoffin, Robert L., Hagens, Shirley J., and Dukellis, Elenc J.
- Jour. Immunol., 1964, 92 (2), 261-274 (Feb.)
227. Serologic Epidemiology of Western Equine and St. Louis Encephalitis Virus Infection in California. I. Persistence of Complement-Fixing Antibody Following Clinical Illness.
- Stallones, Reuel A., Reeves, William C., and Lennette, Edwin H.
- Amer. Jour. Hyg., 1964, 79 (1), 16-28 (Jan.)
228. Antigenic Relationship Between Echovirus Types 29 and 32.
- Schmidt, Nathalie J., Ho, Helen H., King, Carole J., Dennis, Juanita and Lennette, Edwin H.
- Proc. Soc. Exper. Biol. and Med., 1964, 116 (1), 77-80 (May)

Bibliography  
Edwin H. Lennette

229. A Complement-Fixing Antigen for Varicella-Zoster Derived from Infected Cultures of Human Fetal Diploid Cells.
- Schmidt, Nathalie J., Lennette, Edwin H., Shon, Carol W. and Shinomoto, Tak T.
- Proc. Soc. Exper. Biol. and Med., 1964, 116 (1), 144-149 (May)
230. Studies on Filtrates from Cultures of a Psychrophilic Pseudomonas sp. which Inactivate Nonspecific Serum Inhibitors for Certain Hemagglutinating Viruses.
- Schmidt, Nathalie J., Dennis, Juanita and Lennette, Edwin H.
- Jour. Immunol., 1964, 93 (1), 140-147 (July)
231. Neutralizing Activity of Fragments Obtained by Papain Digestion of Viral Antibody.
- Cremer, Natalie E., Riggs, John L., Fujimoto, Frances Y., Hagens, Shirley J., Ota, Margaret I. and Lennette, Edwin H.
- Jour. Immunol., 1964, 93 (2), 283-292 (August)
232. The Sensitivity of Grivet Monkey Kidney Cell Line BS-C-1 for Propagation and Isolation of Certain Human Viruses.
- Schmidt, Nathalie J., Lennette, Edwin H., Shon, Carol W. and Dennis, Juanita
- Amer. Jour. Pub. Hlth., 1964, 54 (4), 1522-1530 (Sept.)
233. Inhibitors of Echovirus and Reovirus Hemagglutination. I. Inhibitors in Tissue Culture Fluids.
- Schmidt, Nathalie J., Dennis, Juanita, Hoffman, Marjorie N. and Lennette, Edwin H.
- Jour. Immunol., 1964, 93 (3), 367-376 (Sept.)
234. Inhibitors of Echovirus and Reovirus Hemagglutination. II. Serum and Phospholipid Inhibitors.
- Schmidt, Nathalie J., Dennis, Juanita, Hoffman, Marjorie N. and Lennette, Edwin H.
- Jour. Immunol., 1964, 93 (3), 377-386 (Sept.)

Bibliography  
Edwin H. Lennette

235. General Principles Underlying Laboratory Diagnosis of Viral and Rickettsial Infections.
- Lennette, Edwin H.
- Diagnostic Procedures for Viral and Rickettsial Diseases,  
Third Edition, Chapter 1, pp. 1-66. The American Public  
Health Association, Inc., New York, 1964.
236. Effect of Antimitotic Agents on Intracellular Reovirus Antigen.
- Spendlove, Rex S., Lennette, Edwin H., Chin, Jean N. and  
Knight, Charles O.
- Cancer Res., 1964, 24 (10), 1826-1833 (November)
237. Simian Virus 40: Isolation of Two Plaque Types.
- Riggs, John L. and Lennette, Edwin H.
- Science, 1965, 147 (3656), 408-409 (January 22)
238. Hemagglutination and Hemagglutination-Inhibition with Adenovirus  
Type 12.
- Schmidt, Nathalie J., King, Carole J. and Lennette, Edwin H.
- Proc. Soc. Exper. Biol. and Med., 1965, 118 (1), 208-211  
(Jan.)
239. The Diagnosis of Rabies by Fluorescent Antibody Method (FRA)  
Employing Immune Hamster Serum.
- Lennette, Edwin H., Woodie, James D., Nakamura, Koichi and  
Magoffin, Robert L.
- Hlth. Lab. Sci., 1965, 2 (1), 24-34 (Jan.)
240. Comparative Sensitivity of Human Fetal Diploid Kidney Cell  
Strains and Monkey Kidney Cell Cultures for Isolation of Certain  
Human Viruses.
- Schmidt, Nathalie J., Ho, Helen H. and Lennette, Edwin H.
- Amer. Jour. Clin. Path., 1965, 43 (4), 297-301 (April)
241. Gel Double Diffusion Studies with Group B and Group A, Type 9,  
Coxsackieviruses. III. Antigen-Antibody Absorption Tests.
- Schmidt, Nathalie J., Lennette, Edwin H. and Dennis, Juanita
- Jour. Immunol., 1965, 94 (4), 482-491 (May)

Bibliography  
Edwin H. Lennette

242. Nonspecific Binding of Complement by Digestion Fragments from Antiviral Gamma Globulin.
- Cremer, Natalie E., Riggs, John L., Lennette, Edwin H. and Jensen, Florence W.
- Science, 1965, 149 (3679), 84-85 (July)
243. Antibody Responses of Rhesus (Macaca mulatta) Monkeys Experimentally Infected with Cocksackieviruses of Group B and Group A, Type 9. I. Antibody Responses within the Cocksackievirus Group.
- Schmidt, Nathalie J., Dennis, Juanita, Lennette, Edwin H. Ho, Helen H. and Shinomoto, Tak T.
- Jour. Immunol., 1965, 95 (1), 54-69 (July)
244. Herpes-Simplex-Virus Encephalitis: Its Possible Association with Reactivated Latent Infection.
- Leider, William, Magoffin, Robert L., Lennette, Edwin H. and Leonards, L. N. R.
- New Eng. Jour. Med., 1965, 273 (7), 341-347 (Aug. 12)
245. On the Alleged Antigenic Relation Between ECHO Virus Types 29 and 32.
- Rosen, Leon, Behbehani, Abbas M., Kamitsuka, Paul S., Kern, Jerome, Lennette, Edwin H., Melnick, Joseph L., Schmidt, Nathalie J. and Wenner, Herbert A.
- Proc. Soc. Exper. Biol. and Med., 1965, 119 (3), 908-910 (July)
246. Immunofluorescent Staining in the Laboratory Diagnosis of Varicella-Zoster Virus Infections.
- Schmidt, Nathalie J., Lennette, Edwin H., Woodie, James D. and Ho, Helen H.
- Jour. Lab. and Clin. Med., 1965, 66 (3), 403-412 (Sept.)
247. Formal Discussion of: A Survey of the Tumor Virus Problem from an Epidemiologic Standpoint.
- Lennette, Edwin H.
- Cancer Res., 1965, 25 (8), 1286-1288 (Sept.)

Bibliography  
Edwin H. Lennette

248. Basic Technics for Virology.

Schmidt, Nathalie J. and Lennette, Edwin H.

Viral and Rickettsial Infections of Man, Fourth Edition,  
Appendix, pp. 1189-1231. J. B. Lippincott Co., Philadelphia,  
1965.

249. An Immunofluorescent Staining Method for Rapid Identification  
of Respiratory Syncytial Virus.

Schieble, Jack H., Lennette, Edwin H. and Kase, Alice

Proc. Soc. Exper. Biol. and Med., 1965, 120 (1), 203-208  
(Oct.)

250. Detection of Adenovirus Type 12 Neoantigen(s) in a Continuous  
Human Amnion Cell Line (FL) by Immunofluorescence.

Riggs, John L., Takemori, Nobuyuki and Lennette, Edwin H.

Proc. Soc. Exper. Biol. and Med., 1965, 120 (3), 832-837  
(Dec.)

251. Difference in Mechanism of Viral Neutralization under In Vitro  
and In Vivo Conditions.

Cremer, Natalie E., Lennette, Edwin H., Hagens, Shirley J.  
and Fujimoto, Frances Y.

Jour. Immunol., 1966, 96 (2), 284-288 (Feb.)

252. Hemagglutination-Inhibiting Antibody Responses in Human Infections  
with Group B Coxsackieviruses.

Schmidt, Nathalie J., Lennette, Edwin H. and Dennis, Juanita.

Jour. Immunol., 1966, 96 (2), 311-318 (Feb.)

253. The Complement-Fixing Antigen of Rubella Virus.

Schmidt, Nathalie J. and Lennette, Edwin H.

Proc. Soc. Exper. Biol. and Med., 1966, 121 (1), 243-250  
(Jan.)

254. Microneutralization Test for the Reoviruses. Application to  
Detection and Assay of Antibodies in Sera of Laboratory Animals.

Schmidt, Nathalie J., Lennette, Edwin H. and Hanahoe, Maureen F.

Proc. Soc. Exper. Biol. and Med., 1966, 121 (4), 1268-1270  
(April)

Bibliography  
Edwin H. Lennette

255. On the Nature of Complement-Fixing Antibodies to Mycoplasma pneumoniae.  
Schmidt, Nathalie J., Lennette, Edwin H., Dennis, Juanita and Gee, Pinkie S.  
Jour. Immunol., 1966, 97 (1), 95-99 (July)
256. Neutralizing, Hemagglutination-Inhibiting and Group Complement-Fixing Antibody Responses in Human Adenovirus Infections.  
Schmidt, Nathalie J., Lennette, Edwin H. and King, Carole J.  
Jour. Immunol., 1966, 97 (1), 64-74 (July)
257. Filter Paper Disc Method of Collecting Whole Blood for Serologic Studies in Children.  
Chin, James, Schmidt, Nathalie J., Lennette, Edwin H. and Hanahoe, Maureen  
Amer. Jour. Epid., 1966, 84 (1), 74-80 (July)
258. A Micro Method for Performing Parainfluenza Virus Neutralization Tests.  
Schmidt, Nathalie J., Lennette, Edwin H. and Hanahoe, Maureen F.  
Proc. Soc. Exper. Biol. and Med., 1966, 122 (4), 1062-1067 (Aug.-Sept.)
259. Production in FL Cells of Infectious and Potentially Infectious Reovirus.  
Spendlove, Rex S., Lennette, Edwin H., Knight, Charles C. and Chin, Jean N.  
Jour. Bact., 1966, 92 (4), 1036-1040 (Oct.)
260. Identification of Rubella Virus Isolates by Immunofluorescent Staining, and a Comparison of the Sensitivity of Three Cell Culture Systems for Recovery of Virus.  
Schmidt, Nathalie J., Lennette, Edwin H., Woodie, James D. and Ho, Helen H.  
Jour. Lab. and Clin. Med., 1966, 68 (3), 502-509 (September)

## Bibliography

Edwin H. Lennette

261. Cold Agglutinins, Eaton Agent, and Respiratory Infections of Children.  
Sussman, Sidney J., Magoffin, Robert L., Lennette, Edwin H. and Schieble, Jack  
Pediatrics, 1966, 38 (4), Part I, 571-577 (October)
262. Rubella Complement-Fixing Antigens Derived from the Fluid and Cellular Phases of Infected BHK-21 Cells: Extraction of Cell-Associated Antigen with Alkaline Buffers.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Immunol., 1966, 97 (6), 815-821 (Dec.)
263. Demonstration of Rubella Complement-Fixing Antigens of Two Distinct Particle Sizes by Gel Filtration on Sephadex G-200.  
Schmidt, Nathalie J., Lennette, Edwin H. and Gee, Pinkie S.  
Proc. Soc. Exper. Biol. and Med., 1966, 123 (3), 758-762 (Dec.)
264. Observations on Antigenic Variants of Echovirus Type 11.  
Schmidt, Nathalie J., Lennette, Edwin H. and Ho, Helen H.  
Proc. Soc. Exper. Biol. and Med., 1966, 123 (3), 696-700 (Dec.)
265. Immunofluorescent Staining in the Laboratory Diagnosis of Colorado Tick Fever.  
Emmons, Richard W. and Lennette, Edwin H.  
Jour. Lab. and Clin. Med., 1966, 68 (6), 923-929 (Dec.)
266. A Probable New Human Picornavirus Associated with Respiratory Disease.  
Schieble, Jack H., Fox, Virginia L., and Lennette, Edwin H.  
Am. Jour. Epid., 1967, 85 (2), 297-310 (May)
267. A Modified Indirect Immunofluorescent Staining Technique for the Demonstration of Rubella Antibodies in Human Sera.  
Lennette, Edwin H., Woodie, James D., and Schmidt, Nathalie J.  
Jour. Lab. and Clin. Med., 1967, 69 (4), 689-695 (Apr.)

Bibliography  
Edwin H. Lennette

268. Antibody Responses of Rhesus (*Macaca mulatta*) Monkeys Experimentally Infected with Coxsackieviruses of Group B and Group A, Type 9. II. Heterotypic Antibody Responses to Echoviruses, Polioviruses and Reovirus Type 1.  
Schmidt, Nathalie J., Dennis, Juanita and Lennette, Edwin H.  
Jour. Immunol., 1967, 98 (5), 1060-1066 (May)
269. Fluorescent Cell Counting as an Assay Method for Respiratory Syncytial Virus.  
Schieble, Jack H., Kase, Alice and Lennette, Edwin H.  
Jour. Virol., 1967, 1 (3), 494-499 (June)
270. Infectivity Assay of Reoviruses: Comparison of Immunofluorescent Cell Count and Plaque Methods.  
McClain, Mary E., Spendlove, Rex S. and Lennette, Edwin H.  
Jour. Immunol., 1967, 98 (6), 1301-1308 (June)
271. Stability of Rubella Complement-Fixing Antigens.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Appl. Micro., 1967, 15 (4), 916-920 (July)
272. The Effect of Gamma Globulin on Acute Respiratory Illness in Military Recruits  
Chir, James, Stallones, Reuel A. and Lennette, Edwin H.  
Amer. Jour. Epid., 1967, 86 (1), 193-198 (July)
273. Isolation of St. Louis Encephalitis Virus from a Naturally-Infected Gray Fox *Urocyon cinereoargenteus*.  
Ermons, Richard W. and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1967, 125, 443-447 (June)
274. Density Gradient Centrifugation Studies on Rubella Complement-Fixing Antigens.  
Schmidt, Nathalie J., Lennette, Edwin H. and Dennis, Juanita  
Jour. Immunol., 1967, 99 (2), 399-405 (Aug.)

Bibliography  
Edwin H. Lennette

275. Additional Evidence of the Relation Between Subacute Inclusion-Body Encephalitis and Measles Virus.  
Freeman, J.M., Magoffin, R.L., Lennette, E.H. and Herndon, R.M.  
The Lancet, 1967, 129-131 (July 15)
276. Serology of Rubella-Comparison of Fluorescent Antibody, Complement Fixation and Neutralization Tests for Diagnosis of Current Infections and Determination of Sero-immunity.  
Lennette, Edwin H., Schmidt, Nathalie J. and Magoffin, Robert L.  
Calif. Med., 1967, 107, 223-231 (September)
277. The Hemagglutination Inhibition Test for Rubella: A Comparison of its Sensitivity to that of Neutralization, Complement Fixation and Fluorescent Antibody Tests for Diagnosis of Infection and Determination of Immunity Status.  
Lennette, Edwin H., Schmidt, Nathalie J. and Magoffin, Robert L.  
Jour. Immunol., 1967, 99 (4), 785-793 (October)
278. Preface  
Sanders, Murray and Lennette, Edwin H.  
Medical and Applied Virology. Proceedings of the Second International Symposium. Sanders, Murray and Lennette, Edwin H., Eds. Warren H. Green, Inc., St. Louis, 1968.
279. Some Observations on the Immunopathology of Virus-Induced Tumors.  
Lennette, Edwin H.  
Jour. Immunol., 1967, 99 (6), 1055-1061.
280. An Immunofluorescent Method for Yaba Virus Assay.  
Taylor, Dee O. N., Klauber, Melville R., Lennette, Edwin H. and Wiener, Anna  
J. Nat. Cancer Inst., 1968. 40 (1) 147-155 (January)
281. D. Viruses. 1. The Preparation of Animal Viruses for Use as Antigens  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Methods in Immunology and Immunochemistry, Volume 1, Preparation of Antigens and Antibodies, Williams, Curtis A. and Chase, Merrill W., Eds., Section 1, D, 1, pp. 87-102. Academic Press, Inc., New York, 1967.

282. In vitro Transformation of Newborn-Hamster Kidney Cells by Simian Adenoviruses.  
Riggs, John L. and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. Med., 1967, 126, 802-806 (Dec.)
283. Isolation of Herpesvirus Hominis from Naturally Infected Pet Skunks.  
Emmons, Richard W. and Lennette, Edwin H.  
Health Lab. Sci., 1968, 5 (1), 31-37 (Jan.)
284. Immunologic Evidence of Measles as an Etiologic Agent in Subacute Sclerosing Panencephalitis.  
Lennette, Edwin H., Magoffin, Robert L. and Freeman, John M.  
Neurol., 1968, 18 (1) Part 2, 21-29 (Jan.)
285. Characterization of Antibodies Produced in Natural and Experimental Coxsackievirus Infections.  
Schmidt, Nathalie J., Lennette, Edwin H. and Dennis, Juanita  
J. Immunol., 1968, 100 (1), 99-106.
286. Cross-Reactivity Between T Antigens of Adenoviral Immunotypes of Proved and Currently Unproved Oncogenic Potential.  
Riggs, John L., Takemori, Nobuyuki and Lennette, Edwin H.  
J. Immunol., 1968, 100 (2), 348-354.
287. Rhinoviruses: The Isolation and Characterization of Three New Serologic Types.  
Schieble, Jack H., Lennette, Edwin H., and Fox, Virginia L.  
Proc. Soc. Exper. Biol. Med., 1968, 127, 324-328.
288. Physical and Immunologic Properties of Rubella Antigens.  
Schmidt, N. J., Lennette, E. H., Gee, P. S. and Dennis, J.  
J. Immunol., 1968, 100 (4), 851-857 (April).
289. Concurrent Administration of Live Adenovirus, Type 4 and Live Poliovirus, Type 1 Vaccines.  
Chin, James, Lennette, Edwin H., Schieble, Jack H., and Magoffin, Robert L.,  
Am. J. Epidemiol., 1968, 87 (3), 633-642 (May).

290. Natural Fatal Infection of an Owl Monkey (Aotus trivirgatus) with Herpes T Virus.  
Emmons, Richard W., Gribble, David H., and Lennette, Edwin H.  
Jour. of Inf. Dis., 1968, 118, 153-159 (April).
291. Viral Oncogenicity and Viral Vaccines--General Comments. National Cancer Institute Monograph No. 29. Virus Vaccine Production, 439-443.  
Lennette, Edwin H.  
Cancer Rsch., 1968, (9), 1825-1828.
292. Hemadsorption and Hemadsorption Inhibition Tests for Rubella Virus.  
Schmidt, Nathalie J., Dennis, Juanita and Lennette, E. H.  
Archiv für die gesamte Virusforschung, 1968, 25, 308-320.
293. Isolation of Western Equine Encephalomyelitis Virus from an Opossum.  
Emmons, Richard W., and Lennette, Edwin H.  
Science, 1969, 163, 945-946 (Feb. 28).
294. Field Evaluation of a Respiratory Syncytial Virus Vaccine and a Trivalent Parainfluenza Virus Vaccine in a Pediatric Population.  
Chin, James, Magoffin, Robert L., Shearer, Lois Ann, Schieble, Jack H. and Lennette, Edwin H.  
Amer. J. Epid., 1969, 89 (4), 449-463 (April).
295. Development and Application of a Hemadsorption and Hemadsorption-Inhibition Test for Rubella Virus.  
Lennette, E. H. and Schmidt, Nathalie J.  
International Symposium on Rubella Vaccines, London, 1968  
Symp. Series immunobiol. Standard., 1969, 11, 109-116  
(Karger, Basel/New York)
296. Localization of Immunoglobulin and Viral Antigen in Rats Infected With Moloney Virus  
Cremer, Natalie E., Taylor, Dee O. N. and Lennette, Edwin H.  
J. Nat. Cancer Inst., 1969, 42 (5), 695-705 (May)
297. Antigens of Rubella Virus  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. J. Dis. Child., 1969, 118, 89-93 (July)

298. Immunological Relationship between Herpes Simplex and Varicella-zoster Viruses Demonstrated by Complement-fixation, Neutralization and Fluorescent Antibody Tests.  
Schmidt, Nathalie J., Lennette, E. H. and Magoffin, R. L.  
J. Gen. Virology, 1969, 4, 321-328 (April)
299. Syncytium-forming Agent isolated from Domestic Cats.  
Riggs, John L., Oshiro, Lyndon S., Taylor, Dee O.N. and Lennette, Edwin H.  
Nature, 1969, 222 (5199), 1190-1191 (June 21)
300. Enzymes Produced by a Pseudomonas Species Which Inactivate Inhibitors of Certain Viral Hemagglutinins. I. Identification and Purification of a Proteinase and Phospholipase C.  
Schmidt, Nathalie J., Gee, Pinkie S., Dennis, Juanita and Lennette, Edwin H.  
Applied Microbiol., 1969, 18 (3), 500-508 (Sept.)
301. Demonstration of Intranuclear T-Antigen by Antisera to Purified Adenovirus 7.  
Jordan, George W., Riggs, John L. and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1969, 132 (1), 10-14, (Oct.)
302. A Plaque Assay for Rubella Virus Based upon Hemadsorption.  
Schmidt, Nathalie J., Lennette, Edwin H. and Dennis, Juanita  
Proc. Soc. Exper. Biol. and Med., 1969, 132 (1), 126-133, (Oct.)
303. Electron Microscopic Studies of Rubella Virus.  
Oshiro, L. S., Schmidt, Nathalie J. and Lennette, E. H.  
J. Gen. Virology, 1969, 5 (2), 205-210 (Sept.)
304. Electron Microscopic Studies on the Localization of Antibodies in Rat Lymph Node Cells Producing Moloney Virus.  
Oshiro, Lyndon S., Cremer, Natalie E., Taylor, Dee O.N. and Lennette, Edwin H.  
J. Nat. Cancer Inst., 1969, 43 (5), 1109-1118 (Nov.)
305. Rubella - Technical Problems in the Performance of Hemagglutination-Inhibition (HI) Tests.  
Lennette, Edwin H. and Schmidt, Nathalie J.  
Calif. Med., 1969, 111, 351-354 (Nov.)

306. T Antigen from Nuclear and Cytoplasmic Extracts from an Adenovirus Type 12 Transformed Cell Line  
Riggs, J. L., Teitz, Y., Cremer, N. E. and Lennette, E. H.  
Proc. Soc. Exper. Biol. and Med., 1969, 132 (2), 527-532 (Nov.)
307. Serologic Diagnosis of Colorado Tick Fever. A Comparison of Complement-Fixation, Immunofluorescence and Plaque-Reduction Methods  
Emmons, Richard W., Dondero, Dale V., Devlin, Veronica and Lennette, Edwin H.  
Amer. Jour. Trop. Med. and Hyg., 1969, 18 (5), 796-802 (Sept.)
308. Antigenic Variants of Coxsackievirus Type A24  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Epidemiol., 1970, 91 (1), 99-109 (Jan.)
309. Demonstration of Viral Antibody Activity in Two Immunoglobulin G Subclasses in Patients with Varicella-Zoster Virus Infection  
Leonard, Larry L., Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Immunol., 1970, 104 (1), 23-27 (Jan.)
310. Antigenic Variation of Rhinovirus Type 22  
Schieble, Jack H., Lennette, Edwin H. and Fox, Virginia L.  
Proc. Soc. Exper. Biol. and Med., 1970, 133 (1), 329-333 (Jan.)
311. Variables of the Rubella Hemagglutination-Inhibition Test System and Their Effect on Antigen and Antibody Titers  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Appl. Microbiol., 1970, 19 (3), 491-504 (Mar.)
312. Complement-Fixing and Fluorescent Antibody Responses To An Attenuated Rubella Virus Vaccine  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Epidemiol., 1970, 91 (4), 351-354 (Apr.)
313. Serologic Surveys of Human Cancer Patients for Antibody to Adenovirus T Antigens  
Gilden, Raymond V., Kern, Jerome, Lee, Yong Ki, Rapp, Fred, Melnick, Joseph L., Riggs, John L., Lennette, Edwin H., Zbar, Berton, Rapp, Herbert J., Turner, Horace C. and Huebner, Robert J.  
Amer. Jour. Epidemiol., 1970, 91 (3), 500-509 (Mar.)

314. Immunofluorescence of Adenovirus Type 7 T-Antigen(s) and Virion Antigens in Infected KB Cells  
Jordan, George W., Riggs, John L. and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1970, 134 (3), 756-762 (July)
315. Studies on Respiratory Disease at Fort Ord, California 1957-1968  
Lennette, Edwin H., Chin, James and Magoffin, Robert L.  
Arch. Environ. Hlth., 1970, 21, 321-327 (Sept.)
316. Enhancement of Reovirus Infectivity by Extracellular Removal or Alteration of the Virus Capsid by Proteolytic Enzymes  
Spendlove, R. S., McClain, Mary E. and Lennette, E.H.  
Jour. Gen. Virol., 1970, 8 (2), 83-94 (Aug.)
317. Complement Fixation and Immunodiffusion Tests for Assay of Hepatitis-Associated "Australia" Antigen and Antibodies.  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Immunol., 1970, 105 (3), 604-613 (Sept.)
318. New Findings in Viral Hepatitis  
Lennette, Edwin H. and Schmidt, Nathalie J.  
California's Health, 1970, 28 (4), 6-7 (Oct.)
319. Natural Herpesvirus Hominis Infection of a Gibbon (Hylobates lar)  
Emmons, Richard W. and Lennette, Edwin H.  
Arch. Ges. Virusforsch., 1970, 31, 215-218
320. Discussion of Preceding Papers  
Lennette, Edwin H.  
Unusual Isolates from Clinical Material, Annals of the New York Academy of Sciences, Kundsens, Ruth B., Ed., Vol. 174, Article 2 pp. 999-1005. New York Academy of Sciences, New York, Oct. 30, 1970.
321. Release of C-Type Particles From Normal Rat Thymus Cultures and Those Infected with Moloney Leukemia Virus  
Teitz, Yael, Lennette, Edwin H., Oshiro, Lyndon S. and Cremer, Natalie E.  
Jour. Natl. Cancer Inst., 1971, 46 (1), 11-23, (Jan.)
322. A Comparison of the Diagnostic Value of Adenoviral Complement-fixing Antigens Prepared from Various Immunotypes  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Clin. Pathol., 1971, 55 (1), 34-39, (Jan.)

## Bibliography

Lennette, Edwin H.

323. Avoidance of Rubella Immunization of Women During or Shortly Before Pregnancy  
Chin, James, Ebbin, Allan J., Wilson, Miriam G. and Lennette, Edwin H.  
J.A.M.A., 1971, 215 (4), 632-634 (Jan. 25)
324. Comparison of Various Methods for Preparation of Viral Serological Antigens from Infected Cell Cultures  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Appl. Microbiol., 1971, 21 (2), 217-226 (Feb.)
325. Complications of Rubella Immunization in Children  
Chin, James, Werner, S. B., Kusumoto, H. Howard and Lennette, Edwin H.  
Calif. Med., 1971, 114 (3), 7-12 (Mar.)
326. Enzymes Produced by a Pseudomonas Species Which Inactivate Inhibitors of Certain Viral Hemagglutinins. II. Effect of a Proteinase and Phospholipase C on Viral Hemagglutinin Inhibitors Present in Human Sera  
Schmidt, Nathalie J., Gee, Pinkie S., Dennis, Juanita and Lennette, Edwin H.  
Jour. Immunol., 1971, 106 (6), 1615-1623 (June)
327. Relative Sensitivity of Gel Diffusion, Complement Fixation, and Immuno-electro-osmophoresis Tests for Detection of Hepatitis-Associated Antigen and Antibody  
Schmidt, Nathalie J., Gee, Pinkie S. and Lennette, Edwin H.  
Appl. Microbiol., 1971, 22, 165-170 (Aug.)
328. Ferritin-labeled Antibody Studies of Feline C-type Particles  
Oshiro, Lyndon S., Riggs, John L., Taylor, Dee, O. N., Lennette, Edwin H. and Huebner, Robert J.  
Cancer Res., 1971, 31, 1100-1110 (Aug.)
329. Quantitation of Immunoglobulin- and Virus-Producing Cells in Rats Infected with Moloney Leukemia Virus  
Cremer, Natalie E., Taylor, Dee O. N. and Lennette, Edwin H.  
Jour. Immunol., 1971, 107 (3), 689-697 (Sept.)
330. Electron Microscopic Studies of Coronavirus  
Oshiro, L. S., Schieble, J. H. and Lennette, E. H.  
Jour. Gen. Virol., 1971, 12, 161-168

331. Rubella Virus Hemagglutination with a Wide Variety of Erythrocyte Species

Schmidt, Nathalie J., Dennis, Juanita and Lennette, Edwin H.

Appl. Microbiol., 1971, 22 (3), 469-470 (Sept.)

332. Sensitivity of a One-Day Complement Fixation Test for Detection of Hepatitis-Associated Antigen

Schmidt, Nathalie J. and Lennette, Edwin H.

Health Lab. Sci., 8 (4), 1971, 238-240 (Oct.)

333. Immunofluorescence Staining of Group B Coxsackieviruses

French, Morris L. V., Schmidt, Nathalie J., Emmons, Richard W. and Lennette, Edwin H.

Appl. Microbiol., 1972, 23 (1), 54-61 (Jan.)

334. Perspectives in Virology--Epilog

Lennette, Edwin H.

From Molecules to Man, Perspectives in Virology VII, Pollard, Morris, Ed., pp. 297-307. Academic Press, New York, 1971.

335. Ein neuer serologischer Test zur Diagnostik der subakuten sklerosierenden Panencephalitis

ter Meulen, V., Katz, M., Leonard, L. L., Lennette, E. H. and Koprowski, H.

Monatsschr. Kinderheilkd., 1971, Band 119, Heft 7, 322-324

336. The Need for Routine Rubella Antibody Testing of Women

Chin, James, Magoffin, Robert L. and Lennette, Edwin H.

Calif. Med., 1972, 116, 9-13 (Mar.)

337. Safety Precautions for Performing Tests for Hepatitis-associated "Australia" Antigen and Antibodies

Schmidt, Nathalie J. and Lennette, Edwin H.

Amer. Jour. Clin. Path., 1972, 57 (4), 526-530 (Apr.)

338. Replication of Feline C-type Virus at the Plasma Membrane of Erythrocytes  
Oshiro, Lyndon S., Taylor, Dee O. N., Riggs, John L. and Lennette, Edwin H.  
J. Natl. Cancer Inst., 1972, 48 (5), 1419-1424 (May)
339. Laboratory Diagnosis of Viral Infections: General Principles  
Lennette, Edwin H.  
Am. J. Clin. Path., 1972, 57 (6), 737-750 (June)
340. Panel Discussion: Laboratory Diagnosis of Viral Infections--Recent Advances and Their Clinical Application  
Lennette, Edwin H. et al  
Am. J. Clin. Path., 1972, 57 (6), 835-845 (June)
341. General Principles Underlying Laboratory Diagnosis of Viral and Rickettsial Infections  
Lennette, Edwin H.  
Diagnostic Procedures for Viral and Rickettsial Infections, Fourth Edition, Lennette, Edwin H. and Schmidt, Nathalie J., Eds., Chapter 1, pp. 1-65. American Public Health Assn., New York, 1969.
342. Clinical Virology: Introduction to Methods  
Lennette, Edwin H., Melnick, Joseph L. and Chanock, Robert M.  
Manual of Clinical Microbiology, First Edition, Blair, John E., Lennette, Edwin H. and Truant, Joseph P., Eds., Chapter 52, pp. 489-497. American Society for Microbiology, Bethesda, 1970.
343. Occurrence and Persistence of "Australia" Antigen Determinants  
Schmidt, Nathalie J., Roberto, Ronald R. and Lennette, Edwin H.  
Infect. Immun., 1972, 6 (1), 1-4 (July)

344. The Effect of 6-Azauridine Upon Subacute Sclerosing Panencephalitis Virus in Tissue Cultures

ter Meulen, V., Leonard, L. L., Lennette, E. H., Katz, M. and Koprowski, H.

Proc. Soc. Exper. Biol. and Med., 1972, 140 (3), 1111-1115 (July)

- 344A. Subacute Sclerosing Panencephalitis: In-Vitro Characterization of Viruses Isolated from Brain Cells in Culture

ter Meulen, Volker, Katz, Michael, Kaëkell, Yonta-M., Barbanti-Brodano, Giuseppe, Koprowski, Hilary and Lennette, Edwin H.

J. Infect. Dis., 1972, 126 (1), 11-17 (July)

345. The Laboratory Diagnosis of Rabies: Review and Prospective

Lennette, Edwin H. and Emmons, Richard W.

Rabies, Nagano, Yasuiti and Davenport, Fred M., Eds., pp. 77-90. University Park Press, Baltimore (Jan.)

346. Recovery and Characterization of a New Simian Herpesvirus from a Fatally Infected Spider Monkey

Hull, R. N., Dwyer, A. C., Holmes, A. W., Nowakowski, E., Deinhardt, F., Lennette, E. H. and Emmons, R. W.

Second International Symposium on Health Aspects of the International Movement of Animals, Summary of the Seminar, Topic III, Scientific Publication No. 235, pp. 137-144. Pan American Health Organization, World Health Organization, Washington, 1972.

347. El Transporte y Uso de Animales no Domesticos: Una Descripcion General

Lennette, Edwin H. and Emmons, Richard W.

Boletin de la Oficina Sanitaria Panamericana, 1972, 73 (2), 124-131 (Aug.)

- 347A. Viral Neutralization in Relation to Antibody Class

Cremer, Natalie E. and Lennette, Edwin H.

Working Conference on Newer Approaches to Investigation and Diagnosis of Viral Diseases, Sponsored by the Japan-United States Cooperative Medical Science Program, Sept. 18-20, 1972, pp. 59-71.

348. Evaluation of Various Antisera and Gels for Detection of Hepatitis-Associated Antigen by Immunodiffusion and Immuno-electrophoresis Tests  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Amer. Jour. Clin. Path., 1972, 58 (3), 317-325 (Sept.)
349. An Anemia-Inducing Virus Derived from Tumors Caused by Murine Sarcoma Virus--Moloney  
Taylor, Dee O. N., Cremer, Natalie E., Oshiro, Lyndon S., and Lennette, Edwin H.  
Jour. Natl. Cancer Inst., 1972, 49 (3), 829-845 (Sept.)
350. Complement Fixation Tests for Detection of Antigen and Antibody Associated with Viral Hepatitis, Type B  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Hepatitis and Blood Transfusion, Vyas, Girish N., Perkins, Herbert A. and Schmid, Rudi S., Eds., pp. 125-132. Grune and Stratton, Inc., New York, 1972
351. Computer Assisted Analysis of a Carrier Culture Infected with Moloney Leukemia Virus  
ter Meulen, Volker, Bartels, Peter H., Bahr, Gunter F., Bibbo Marluce, Cremer, Natalie E, Lennette, Edwin H. and Wied, George L.  
Acta Cytologica, 1972, 16 (5), 454-463 (Sept.)
352. Rubella Vaccination and Pregnancy  
Ebbin, A. J., Wilson, M. G., Wehrle, P. F., Chin, J., Emmons, R. W. and Lennette, E. H.  
Lancet, 1972, 481-482 (Sept. 2)
353. Intra-erythrocytic Location of Colorado Tick Fever Virus  
Emmons, R. W., Oshiro, L. S., Johnson, H. N. and Lennette, E. H.  
Jour. Gen. Virol, 1972, 17, 185-195
354. Health Problems Associated with the Transportation and Use of Nondomestic Animals: An Overview  
Lennette, Edwin H. and Emmons, Richard W.  
Pan. Am. Hlth. Org., WHO, 1972, Scientific Publication No. 235, pp. 3-9.
- 354A. Contributions of the Biological Sciences to Human Welfare,  
Chapter I: "Introduction"

355. Advances in the Serodiagnosis of Viral Infections

Schmidt, Nathalie J. and Lennette, Edwin H.

Progress in Medical Virology, Melnick, Joseph L., Ed., Volume 15,  
pp. 244-308. S. Karger, Basel, 1973.

356. A Type-C Virus in Human Rhabdomyosarcoma Cells After Inoculation Into NIH Swiss Mice Treated with Antithymocyte Serum  
Todaro, George J., Arnstein, Paul, Parks, Wade P., Lennette, Edwin H. and Huebner, Robert J.  
Proc. Natl. Acad. Sci., 1973, 70 (3), 859-862 (Mar.)
357. Neutralization, Fluorescent Antibody and Complement Fixation Tests for Rubella  
Lennette, Edwin H. and Schmidt, Nathalie J.  
Rubella. First Annual Symposium of the Eastern Pennsylvania Branch, American Society for Microbiology, Friedman, Herman and Prier, James E., Eds., Chapter 3, pp. 18-32. Charles C. Thomas, Springfield, 1973.
358. Electron Microscopic Identification of Papova Virus in Laryngeal Papilloma  
Boyle, William F., Riggs, John L., Oshiro, Lyndon S. and Lennette, Edwin H.  
Laryngoscope, 1973, Vol. LXXXIII (7), 1102-1108 (July)
359. Demonstration of Rubella IgM Antibody by Indirect Fluorescent Antibody Staining, Sucrose Density Gradient Centrifugation and Mercaptoethanol Reduction  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Intervirology, 1973, I, 48-59
360. Prevalence of Type-C Virus and Antibodies in Normal Cats and Cats with Neoplasia  
Riggs, John L., Oshiro, Lyndon S., Taylor, Dee O. N. and Lennette, Edwin H.  
Jour. Natl. Cancer Inst., 1973, 51 (2), 449-454 (Aug.)
361. Potential Hazards Posed by Nonviral Agents. Session I  
Lennette, Edwin H.  
Biohazards in Biological Research, 1973, A. Hellman, M. N. Oxman and R. Pollack, Eds. Published by Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, pp. 47-62.
- 361A. Cytomegalovirus Infection  
Chin, Wing, Magoffin, Robert, Frierson, J. Gordon, and Lennette, Edwin H.  
J.A.M.A., 1973, 225 (7), 740-741 (Aug. 13)

362. IgM Production in Rats Infected with Moloney Leukemia Virus  
Cremer, Natalie E., Taylor, Dee O. N., Lennette, Edwin H.  
and Hagens, Shirley J.  
Jour. Natl. Cancer Inst., 1973, 51 (3), 905-915 (Sept.)
363. Virologic and Immunologic Aspects of Major Oral Ulcerations  
Lennette, E. H. and Magoffin, Robert L.  
Jour. Amer Dent. Assoc., 1973, 87, 1055-1073 (Oct.)
364. Association of Group B Coxsackieviruses with Cases of Pericarditis,  
Myocarditis, or Pleurodynia by Demonstration of Immunoglobulin M  
Antibody  
Schmidt, Nathalie J., Magoffin, Robert L. and Lennette, Edwin H.  
Infect. and Immun., 1973, 8 (3), 341-348 (Sept.)
365. Basic Considerations in Rubella Serology  
Principles and Components of Rubella HI Test Systems  
Microtiter Test System  
Rubella Hemagglutination Inhibition Test Procedure  
Interpretation of Serologic Tests for Rubella  
Lennette, Edwin H. and Schmidt, Nathalie J.  
Principles and Performance of the Rubella Hemagglutination Inhibition  
Test (Loose Leaf), Lennette, Edwin H. and Schmidt, Nathalie J., Eds.,  
pp. 1-33, Commission on Continuing Education, Council on Microbiology.  
American Society of Clinical Pathologists, Chicago, 1973.
366. Serodiagnosis of Viral Infections  
Lennette, Edwin H. and Schmidt, Nathalie J.  
Anatomic and Clinical Pathology, International Congress Series  
No. 285, Proceedings of the VIII World Congress of Anatomic and  
Clinical Pathology, Munich, 12-16 Sept. 1972, Chapter V, pp. 168-171.  
Excerpta Medica, Amsterdam.
367. Colorado Tick Fever  
Emmons, Richard W. and Lennette, Edwin H.  
Arch. Intern. Med., 1973, 132, 629 (Oct.)
- 367A. Carrier Cultures of Human Fetal Diploid Cells Infected with Coxsackievirus  
Type B2  
Maverakis, N. H., Schmidt, Nathalie J., Riggs, J. L. and  
Lennette, E. H.  
Arch. Ges. Virusforsch., 1973, 43, 289-296
- 367B. Cultures of Tissues from Patients with Amyotrophic Lateral Sclerosis  
Cremer, Natalie E., Oshiro, Lyndon S., Norris, Forbes H., Jr.,  
and Lennette, Edwin H.  
Arch. Neurol., 1973, 29, 331-333 (Nov.)

## Bibliography

Edwin H. Lennette

368. Sensitivity of Radioimmunoassay for Hepatitis B Antigen in Diagnostic and Survey Work  
Schmidt, Nathalie J., Forghani, Bagher and Lennette, Edwin H.  
Health Lab. Sci., 1974, 11 (1), 4-7 (Jan.)
369. Preface  
Zeman, Wolfgang and Lennette, Edwin H.  
Slow Virus Diseases, Zeman, Wolfgang and Lennette, Edwin H., Eds., American Association of Pathologists and Bacteriologists, Washington, D. C., 1973, pp. vii-viii. Williams and Wilkins Co., Baltimore, 1974.
370. Propagation of Human Tumors in Antithymocyte Serum-Treated Mice  
Arnstein, Paul, Taylor, Dee O. N., Nelson-Rees, Walter A., Huebner, Robert J. and Lennette, Edwin H.  
Jour. Natl. Cancer Inst., 1974, 52 (1), 71-84 (Jan.)
371. An Apparently New Enterovirus Isolated from Patients with Disease of the Central Nervous System  
Schmidt, Nathalie J., Lennette, Edwin H. and Ho, Helen H.  
Jour. Infect. Dis., 1974, 129 (3), 304-309 (Mar.)
372. Ferritin-labelled Antibody Study of RD-114 Virus  
Oshiro, L. S., Riggs, J. L., Lennette, E. H. and McAllister, R. M.  
Jour. Gen. Virol., 1974, 22 (2), 277-280 (Feb.)
373. Clinical Virology: Introduction to Methods  
Lennette, Edwin H., Melnick, Joseph L. and Magoffin, Robert L.  
Manual of Clinical Microbiology, Lennette, Edwin H., Spaulding, Earle H. and Truant, Joseph P., Eds., Second Edition, Chapter 71, pp. 667-677. The American Society for Microbiology, Washington, 1974.
374. The Epidemiology of Influenza in California, 1968-1973  
Chin, James, Magoffin, Robert L. and Lennette, Edwin H.  
West. Jour. Med., 1974, 121 (2), 94-99 (Aug.)

## Bibliography

Edwin H. Lennette

375. Solid Phase Radioimmunoassay for Identification of Herpesvirus hominis Types 1 and 2 from Clinical Materials  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Appl. Microbiol., 1974, 28 (4), 661-667 (Oct.)
376. Immunofluorescent Studies of RD-114 Virus Replication in Cell Culture  
Riggs, J. L., McAllister, R. M. and Lennette, E. H.  
Jour. Gen. Virol., 1974, 25 (1), 21-29 (Oct.)
377. Atypical Demyelinating Disease  
Adams, J. M., Brown, W. J., Cremer, N. E., Eberle, E. D., Fewster, M. E. and Lennette, E. H.  
Jour. Neurol., Neurosurg. and Psychiatry, 1974, 37 (8), 874-878 (Aug.)
378. Antiviral Antibodies in Rheumatoid Synovial Fluid and Cryoprecipitates  
Cremer, Natalie E., Hurwitz, D., Quismorio, F. P., Lennette, E. H. and Friou, G. J.  
Clin. Exper. Immunol., 1974, 18 (1), 27-37 (Sept.)
379. Recovery of Murine Xenotropic Type-C Virus from C57L Mice  
Arnstein, Paul, Levy, Jay A., Oshiro, Lyndon S., Price, Paul J., Suk, William and Lennette, Edwin H.  
Jour. Natl. Cancer Inst., 1974, 53 (6), 1787-1792 (Dec.)
380. Rhinoviruses: Antigenic Study of the Prototype Virus Strains  
Schieble, Jack H., Fox, Virginia L., Lester, Florence and Lennette, Edwin H.  
Proc. Soc. Exper. Biol. and Med., 1974, 147 (2), 541-545 (Nov.)
381. Complement-Fixing Antibody in Human Sera Reactive with Viral and Soluble Antigens of Cytomegalovirus  
Cremer, Natalie E., Schmidt, Nathalie J., Jensen, Florence, Hoffman, Marjorie, Oshiro, Lyndon S. and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1975, 1 (3), 262-267 (Mar.)

382. Perspectives in Virology: Vaccinations  
Lennette, Edwin H.  
Perspectives in Virology IX. Antiviral Mechanisms, Pollard, Morris, Ed., Chapter 1, pp. 1-8. Academic Press, New York, 1975.
383. Chronic Progressive Panencephalitis Due to Rubella Virus Simulating Subacute Sclerosing Panencephalitis  
Weil, Marvin L., Itabashi, Hideo H., Cremer, Natalie E., Oshiro, Lyndon S., Lennette, Edwin H. and Carnay, Laurence  
New Eng. Jour. Med., 1975, 292, 994-998 (May 8)
384. Neutralization Kinetics of Western Equine Encephalitis Virus by Antibody Fragments  
Cremer, Natalie E., Riggs, John L. and Lennette, Edwin H.  
Immunochemistry, 1975, 12 (6/7), 597-601 (July)
385. Introduction  
Lennette, Edwin H. and McManus, J. F. A.  
The Science of Life: Contributions of Biology to Human Welfare, Fisher, K. D. and Nixon, A. U., Eds., Chapter 1, pp. 1-13. Plenum Press, New York, 1975.
386. Section IV. New Vaccines. Introduction  
Lennette, Edwin H.  
Microbiology--1975, Schlessinger, David, Ed., page 399. American Society for Microbiology, Washington, 1975.
387. Rapid Diagnosis of Mumps Virus Infections by Immunofluorescence Methods  
Lennette, David A., Emmons, Richard W. and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1975, 2 (2), 81-84 (Aug.)
388. Neutralizing Antibody Responses to Varicella-Zoster Virus  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Infect. and Immun., 1975, 12 (3), 606-613 (Sept.)

389. Propagation and Isolation of Group A Coxsackieviruses in RD Cells  
Schmidt, Nathalie J., Ho, Helen H. and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1975, 2 (3), 183-185 (Sept.)
- 389A. Old Dog Encephalitis and Demyelinating Diseases in Man  
Adams, J. M., Brown, W. J., Snow, H. D., Lincoln, S. D.,  
Sears, A. W., Jr., Barenfus, M., Holliday, T. A., Cremer,  
N. E. and Lennette, E. H.  
Vet. Pathol., 1975, 12 (3), 220-226
390. Type Specificity of Complement-Requiring and Immunoglobulin M Neutra-  
lizing Antibody in Initial Herpes Simplex Virus Infections of Humans  
Schmidt, Nathalie J., Forghani, Bagher and Lennette, Edwin H.  
Infect. and Immun., 1975, 12 (14), 728-732 (Oct.)
391. Cellular Immunity and SSPE - Summary of the Conference  
Lennette, Edwin H.  
Arch. Neurol., 1975, 32 (7), 488-504 (July)
392. Solid Phase Radioimmunoassay for Typing Herpes Simplex Viral Antibodies  
in Human Sera  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1975, 2 (5), 410-418 (Nov.)
393. Isolation of Rubella Virus from Brain in Chronic Progressive Panencephalitis  
Cremer, Natalie E., Oshiro, L. S., Weil, M. L., Lennette, E. H.,  
Itabashi, H. H. and Carnay, L.  
Jour. Gen. Virol., 1975, 29 (2), 143-153 (Nov.)
394. Viruslike Particles in Muscle from a Patient with Amyotrophic Lateral  
Sclerosis  
Oshiro, Lyndon S., Cremer, Natalie E., Norris, Forbes H., Jr.  
and Lennette, Edwin H.  
Neurol., 1976, 26 (1), 57-60 (Jan.)
395. Comparative Sensitivity of the BGM Cell Line for Isolation of Enteric Viruses  
Schmidt, Nathalie J., Ho, Helen H. and Lennette, Edwin H.  
Health Lab. Sci., 1976, 13 (2), 115-117 (Apr.)

## Bibliography

Edwin H. Lennette

396. Plaque Reduction Neutralization Test for Human Cytomegalovirus Based Upon Enhanced Uptake of Neutral Red by Virus-Infected Cells  
Schmidt, Nathalie J., Dennis, Juanita and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1976, 4 (1), 61-66 (July)
397. Improved Yields of Cell-Free Varicella-Zoster Virus  
Schmidt, Nathalie J. and Lennette, Edwin H.  
Infect. and Immun., 1976, 14 (3), 709-715 (Sept.)
398. Antisera to Human Cytomegalovirus Produced in Hamsters: Reactivity in Radioimmunoassay and Other Antibody Assay Systems  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Infect. and Immun., 1976, 14 (5), 1184-1190 (Nov.)
399. Sensitivity of a Radioimmunoassay Method for Detection of Certain Viral Antibodies in Sera and Cerebrospinal Fluids  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1976, 4 (6), 470-478 (Dec.)
400. Induction of Lymphoma and Associated Xenotropic Type C Virus in C57L Mice by Whole-Body Irradiation  
Arnstein, Paul, Riggs, John L., Oshiro, Lyndon S., Huebner, Robert J. and Lennette, Edwin H.  
Jour. Natl. Cancer Inst., 1976, 57 (5), 1085-1090 (Nov.)
401. Part VI. Perspectives: An Appraisal of Need. Epidemiology  
Lennette, Edwin H.  
Viruses in Water, Berg, Gerald, Bodily, Howard L., Lennette, Edwin H., Melnick, Joseph L. and Metcalf, Theodore G., Eds., page 252. American Public Health Association, Inc., Washington, 1976.
402. Radioimmunoassay Inhibition Method for Confirming the Specificity of Positive Hepatitis B Surface Antigen Reactions and for Survey of Antibodies to the Antigen  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Vox. Sang., 1977, 32 (3), 125-130 (Mar.)

403. Complement-Fixing Reactivity of Varicella-Zoster Virus Subunit Antigens with Sera from Homotypic Infections and Heterotypic Herpes Simplex Virus Infections  
Schmidt, Nathalie J., Dennis, Juanita and Lennette, Edwin H.  
Infect. and Immun., 1977, 15 (3), 850-854 (Mar.)
404. Complications and Immunological Studies of Measles Virus Infection in Antithymocyte-Treated Hamsters  
Cremer, Natalie E., Hagens, Shirley J., Taylor, Dee O. N. and Lennette, Edwin H.  
Infect. and Immun., 1977, 16 (1), 155-162 (Apr.)
405. Distinction Between Envelope Antigens of Murine Xenotropic and Ecotropic Type C Viruses by Immunoelectron Microscopy  
Oshiro, L. S., Levy, J. A., Riggs, J. L. and Lennette, E. H.  
Jour. Gen. Virol., 1977, 35 (2), 317-323 (May)
406. Classic Slow Virus Diseases  
Lennette, E. H.  
Bull. Pan Am. Health Org., 1977, 11 (2), 157-161
407. Rocky Mountain Spotted Fever (Editorial)  
Lennette, Edwin H.  
New Eng. Jour. Med., 1977, 297 (16), 884-885 (Oct. 20)
408. Anti-Complement Immunofluorescence Test for Antibodies to Human Cytomegalovirus  
Kettering, James D., Schmidt, Nathalie J., Gallo, Dana and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1977, 6 (6), 627-632 (Dec.)
409. Improved Glycine-Extracted Complement-Fixing Antigen for Human Cytomegalovirus  
Kettering, James D., Schmidt, Nathalie J. and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1977, 6 (6), 647-649 (Dec.)

410. Problems Posed to Man by Viruses in Municipal Wastes  
Lennette, E. H.  
Virus Aspects of Applying Municipal Waste to Land, Baldwin, L. B., Davidson, J. M. and Gerber, J. F., Eds., pp. 1-7, University of Florida, Gainesville, 1977.
411. Radioimmunoassay of Measles Virus Antigen and Antibody in SSPE Brain Tissue  
Forghani, Bagher, Schmidt, Nathalie J. and Lennette, Edwin H.  
Proc. Soc. Exp. Biol. and Med., 1978, 157 (2), 268-272 (Feb.)
412. The Development of Colorado Tick Fever Virus Within Cells of the Haemopoietic System  
Oshiro, L. S., Dondero, D. V., Emmons, R. W. and Lennette, E. H.  
Jour. Gen. Virol., 1978, 39 (1), 73-79 (Apr.)
413. Comparison of Immunofluorescence and Immunoperoxidase Staining for Identification of Rubella Virus Isolates  
Schmidt, Nathalie J., Dennis, Juanita and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1978, 7 (6), 576-583 (June)
414. Analysis of Antibody Assay Methods and Classes of Viral Antibodies in Serodiagnosis of Cytomegalovirus Infection  
Cremer, Natalie E., Hoffman, Marjorie and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1978, 8 (2), 153-159 (Aug.)
415. Role of Rheumatoid Factor in Complement Fixation and Indirect Hemagglutination Tests for Immunoglobulin M Antibody to Cytomegalovirus  
Cremer, Natalie E., Hoffman, Marjorie and Lennette, Edwin H.  
Jour. Clin. Microbiol., 1978, 8 (2), 160-165 (Aug.)
416. Photochemical Inactivation of DNA and RNA Viruses by Psoralen Derivatives  
Hanson, Carl Veith, Riggs, John L. and Lennette, Edwin H.  
Jour. Gen. Virol., 1978, 40 (2), 345-358 (Aug.)

417. Comparative Sensitivity of Various Cell Culture Systems for Isolation of Viruses from Wastewater and Fecal Samples

Schmidt, Nathalie J., Ho, Helen H., Riggs, John L. and Lennette, Edwin H.

Appl. Environ. Microbiol., 1978, 36 (3), 480-486 (Sept.)

418. Overview--Health Considerations Associated with Land Treatment of Wastewater Systems Compared with Other Human Activities. Comparison of Health Considerations for Land Treatment of Wastewater

Lennette, Edwin H. and Spath, David P.

State of Knowledge in Land Treatment of Wastewater, Vol. 1, pp. 27-34. International Symposium, 20-25 Aug. 1978, Hanover, N. H. U. S. Army Corps of Engineers, Cold Regions Research and Engineering Laboratory, Hanover, 1978.

419. Possible Pitfalls in the Study of IgG Receptors Produced by Herpesvirus-Infected Cells

Forghani, B., Schmidt, Nathalie J. and Lennette, E. H.

Arch. Virol., 1979, 60 (2), 167-169

420. Immunoperoxidase Staining for Detection of Colorado Tick Fever Virus, and a Study of Congenital Infection in the Mouse

Desmond, Edward P., Schmidt, Nathalie J. and Lennette, Edwin H.

Amer. Jour. Trop. Med. and Hyg., 1979, 28 (4), 729-732

421. Recombinant DNA: A Public Health Viewpoint

Lennette, E. H.

Recombinant DNA and Genetic Experimentation, Morgan, Joan and Whelan, W. J., Eds., pp. 261-270. Pergamon Press, Oxford, U.K., 1979.

422. Future Prospects of Tissue Culture in Microbiology

Lennette, Edwin H. and Schmidt, Nathalie J.

Practical Tissue Culture Applications, Maramorosch, Karl and Hirumi, Hiroyuki, Eds., Chapter 27, pp. 409-422. Academic Press, Inc. New York, 1979.

Bibliography  
Edwin H. Lennette

423. Simian Virus Nomenclature, 1980

Kalter, S. S., Ablashi, Dharam, España, Carlos, Heberling, Richard L., Hull, Robert N., Lennette, Edwin H., Malherbe, Hubert N., McConnell, Stewart and Yohn, David S.

Intervirology, 1980, 13 (6), 317-330

424. Perspectives in Medical Virology

Lennette, Edwin H.

Perspectives in Virology XI, Pollard, Morris, Ed., pp. 109-114.  
Alan R. Liss, Inc., New York, 1981.

425. Viral Respiratory Diseases: Vaccines and Antivirals

Lennette, Edwin H.

Bull. WHO, 1981, 59 (3), 305-324

426. Viral Respiratory Diseases

Report of a WHO Scientific Group

World Health Organization Technical Report Series 642. World Health Organization, Geneva, 1980, 1-63.

427. Newer Methods for the Detection of Primate Viruses.

Lennette, Edwin H. and Schmidt, Nathalie J.

Chapter in Viral and Immunological Diseases in Nonhuman Primates.  
Monographs in Primatology, Vol. 2. Kalter, S. S., Ed., pp. 149-160,  
Alan R. Liss, Inc., New York, 1983



APPENDIX C

*Distinguished scientist, teacher and international leader in virology, he has excelled in the development of laboratory technology which reveals the complexities of the viral diseases of man and provides mechanisms for their control.*

EDWIN H. LENNETTE has dedicated his career to the development of laboratory technology for the detection and identification of viral diseases of mankind. He has been in the forefront of the important discoveries of new viruses and the development of new methods for their detection and identification.

His enthusiasm and widespread interest have contributed to the body of knowledge and influenced laboratory technology for nearly every viral agent known to cause disease in man. His studies on influenza vaccine have added greatly to present knowledge and to the processes currently used in vaccine production and application. A host of developments coming from his laboratory has also contributed greatly to the usefulness of tissue cultures in diagnostic laboratories.

Dr. Lennette has also given unstintingly of his time to activities of many commissions, councils and committees of both the federal government and international agencies. His advice is constantly sought on a wide variety of problems and programs concerning viral diseases.

He has developed one of the outstanding viral diagnostic, teaching and research laboratories in the California State Department of Public Health. For over two decades his laboratory has attracted hundreds of scientists from every continent, who come to learn procedures for the detection and identification of viruses. Through his teaching and prodigious writing, viral diagnostic services have been developed around the world—a distinguished contribution to the monitoring and control of epidemics.

## APPENDIX D

## Presentation of the Wellcome Award

New Orleans, Louisiana

September 30, 1986

Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)

The man we honor this evening has represented in his person the history, flowering, and maturity of diagnostic virology. Ed Lennette's name is synonymous with excellence in this field and he has been an authority in it for the lifetimes of many of the people in this room. A native of the great state of Pennsylvania, Pittsburgh to be exact, Ed went to the University of Chicago, then as now an intellectual center, from which he graduated in 1931. In quick succession he received a Ph.D. from the University of Chicago in 1935, and an MD from Rush Medical College in 1936. After an internship in Chicago and some additional time at the University of Chicago, Ed went to Washington University in St. Louis where he did research in polio. 1939-1946 were formative years in Ed's life. As staff member of the Rockefeller Foundation he took part in studies of influenza, yellow fever and other viral diseases in Brazil and the United States. Finally, in 1947 he came to California to head the California Department of Health's new Viral and Rickettsial Disease Laboratory. As the cliché goes, the rest is history.

At Berkeley Ed began to set the standards for all diagnostic labs. Through his books, which became bibles for virologists, he founded the field of diagnostic virology. Just as important he showed us by the innumerable publications through him and his associates that a diagnostic

virology laboratory could also be a research laboratory contributing importantly to virology, to epidemiology, to public health, and to medicine.

Ed's prior honors are too many to mention here. The respect and affection in which he is held by his colleagues are so universal as to almost not require noting. He has been our leader for so long that he is an institution. Nevertheless, it is the amalgam of all these facts that we recognize here tonight. Ladies and gentlemen, the 1986 Pan American Groups for Rapid Viral Diagnosis Wellcome Award in Rapid Viral Diagnosis goes to Edwin H. Lennette, the father of our profession.

## Distinguished Alumnus: Edwin H. Lennette, M.D., Ph.D.

The Rush Medical College Alumni Association's highest honor was awarded this year to Edwin H. Lennette, M.D. '36.

In introducing Dr. Lennette, George J. Hummer, M.D. '37, recalled that even back in medical school, "Eddie had viruses on his mind. Viruses to the rest of us were a very nebulous thing — they hadn't been seen by anybody. But to Eddie, they were the real thing."

Dr. Lennette went on to become the primary moving force in the establishment of public health virology, and a leading contributor to the understanding and treatment of viral and Rickettsial infections.

After graduation from Rush he taught and did research in Chicago for several years. He then joined the international health division of the Rockefeller Foundation, where his assignments included influenza studies, yellow fever research in Brazil, and, eventually, an appointment with the California Department of Public Health.

He held a series of prominent positions with the department, at various times directing its cancer research, laboratory and biomedical laboratory programs. He headed the Viral and Rickettsial Disease Laboratory of the Department of Health Services for 31 years and, under his direction, it became known as the best in the country. The laboratory was instrumental in developing specific diagnostic tests for difficult-to-identify viruses, thereby helping to monitor and control epidemics around the world. His many honors include the American Public Health Association's Bronfman Award and the Wyeth Award in Clinical Microbiology.

Although semi-retired since 1978, Dr. Lennette continues to teach and to serve on a variety of medical boards. He is president of the California Public Health Foundation and president of the board of directors of the Peralta Cancer

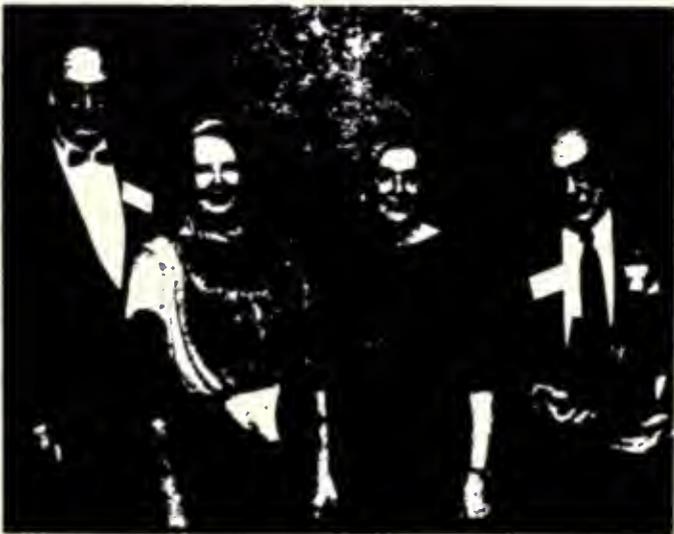
Research Institute in Oakland, California. He is an active member of a number of medical societies and serves on the editorial board of five journals. He's also president of the United States subsidiary of Virion, Inc., a Swiss manufacturer of microbiologic diagnostic reagents.

Dr. Lennette called the award "a high point in my career" and reflected on the development of the field of virology during his lifetime.

"When I entered the field of virology, there was not even a textbook. We didn't even know what we were working with" until the advent of the electron microscope in the 1930s, he recalled. Even then, resolution was poor, and it has only been in recent years that researchers could see viruses in detail.

"In the 1930s, no one knew what a virus was, what the nature of the animal might be," Dr. Lennette continued. One theory was that it was a parasite that had lost most of its characteristics through evolution; the other was that viruses were genes that broke loose in the cell and caused infections. The advent of the electron microscope, ultracentrifugation and tissue cultures has reaffirmed the second belief. "There is no lack of entities within the cell which could become a virus," he said.

Researchers have followed two approaches in the development of vaccinations: either disassembling the virus or removing the genome that produces the peptides which confer immunity. "We've come a long way, to where we know viruses are involved not only in infectious diseases but also in neurological diseases like cancer," Dr. Lennette concluded. "This is a big difference from the 1930s, when if you didn't know the causation of a disease, you automatically put it in this waste basket known as 'viruses.'" ■

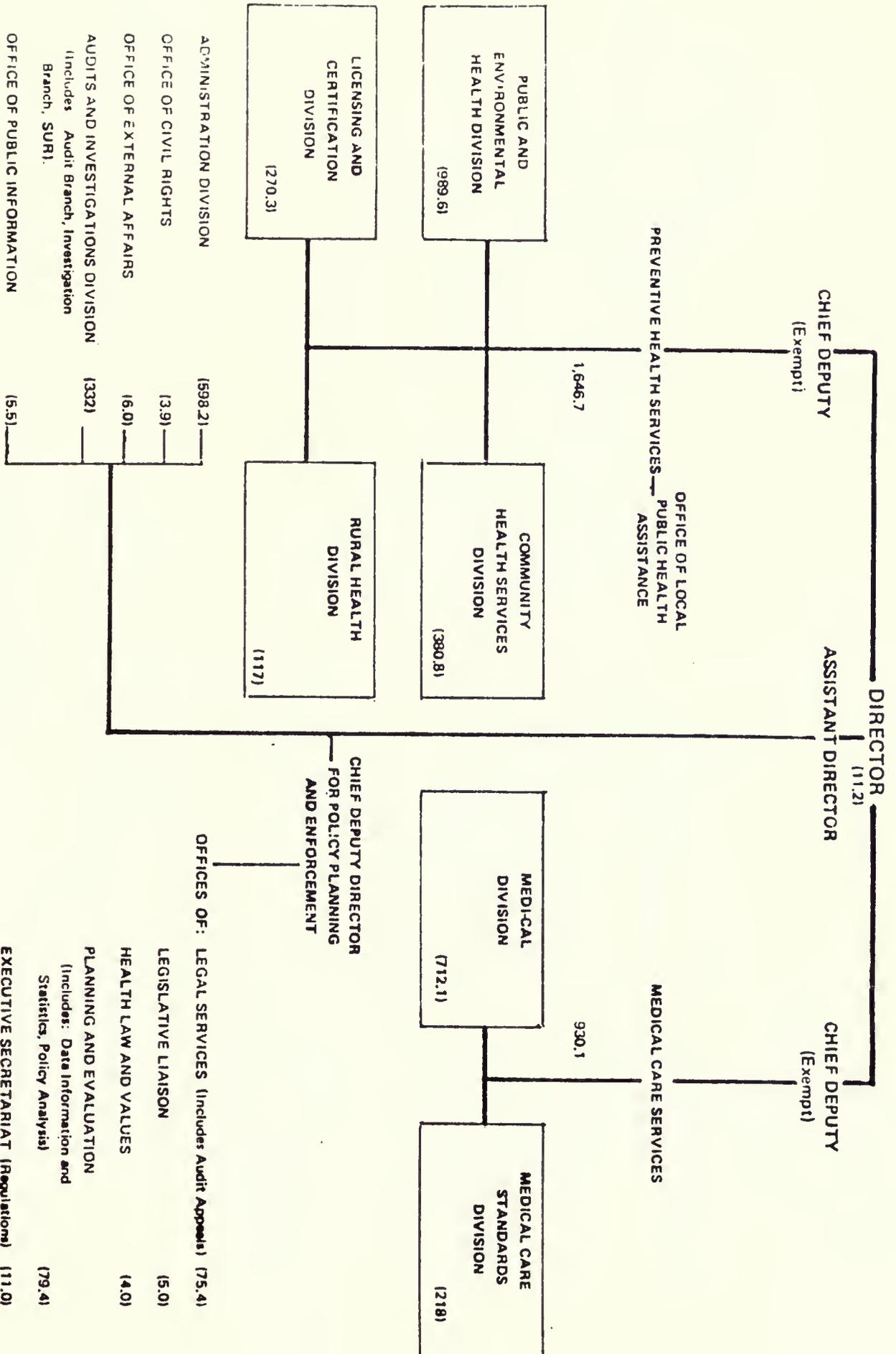


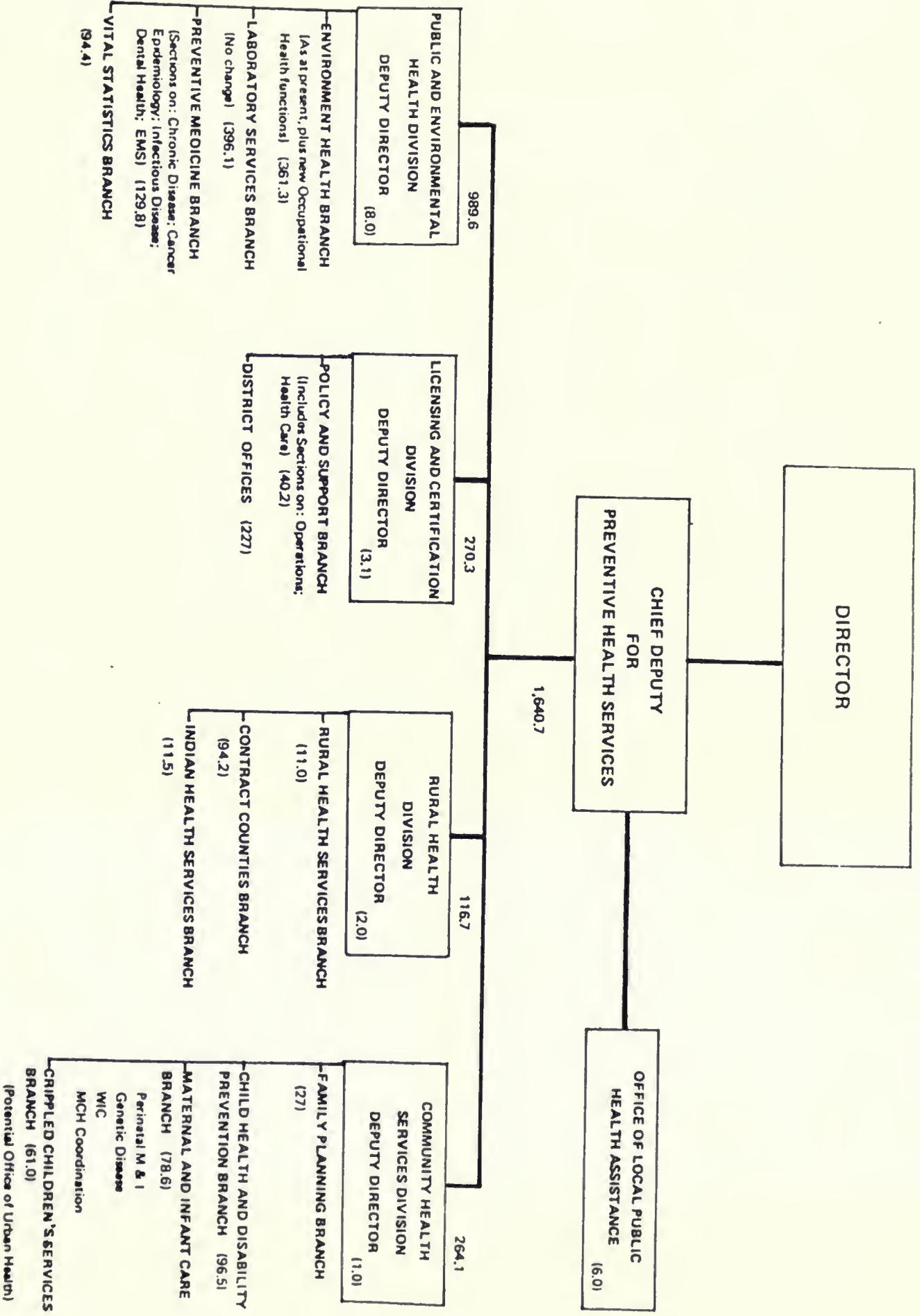
George J. Hummer, M.D. '37, Mrs. Hummer, Melda Parkinson and Edwin H. Lennette, M.D. '36, Ph.D.



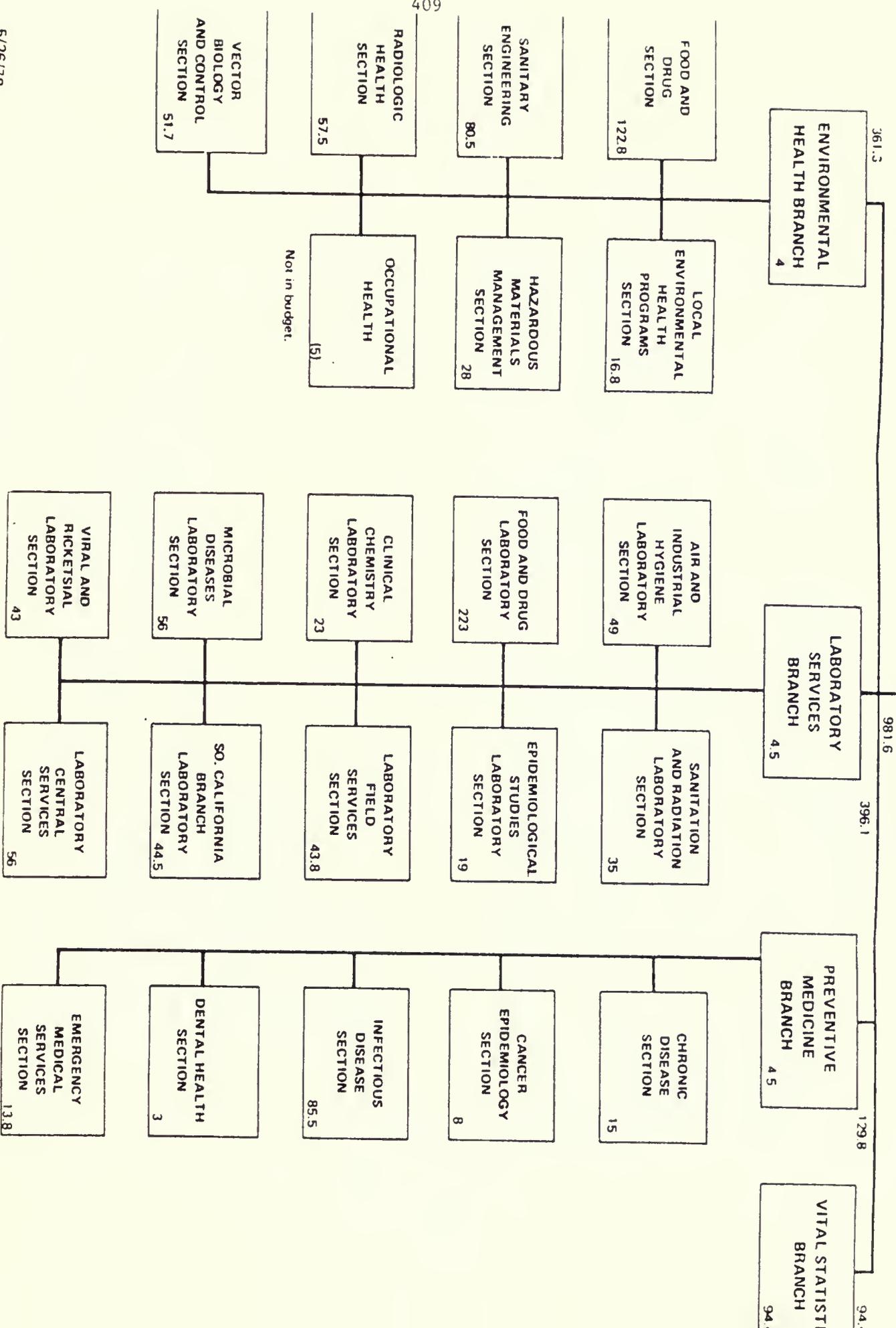
Distinguished alumnus Edwin H. Lennette, M.D. '36 (right) chats with Donald Nash, M.D. '76.

ORGANIZATION CHARTS OF THE CALIFORNIA DEPARTMENT OF HEALTH SERVICES, 1977 and 1978





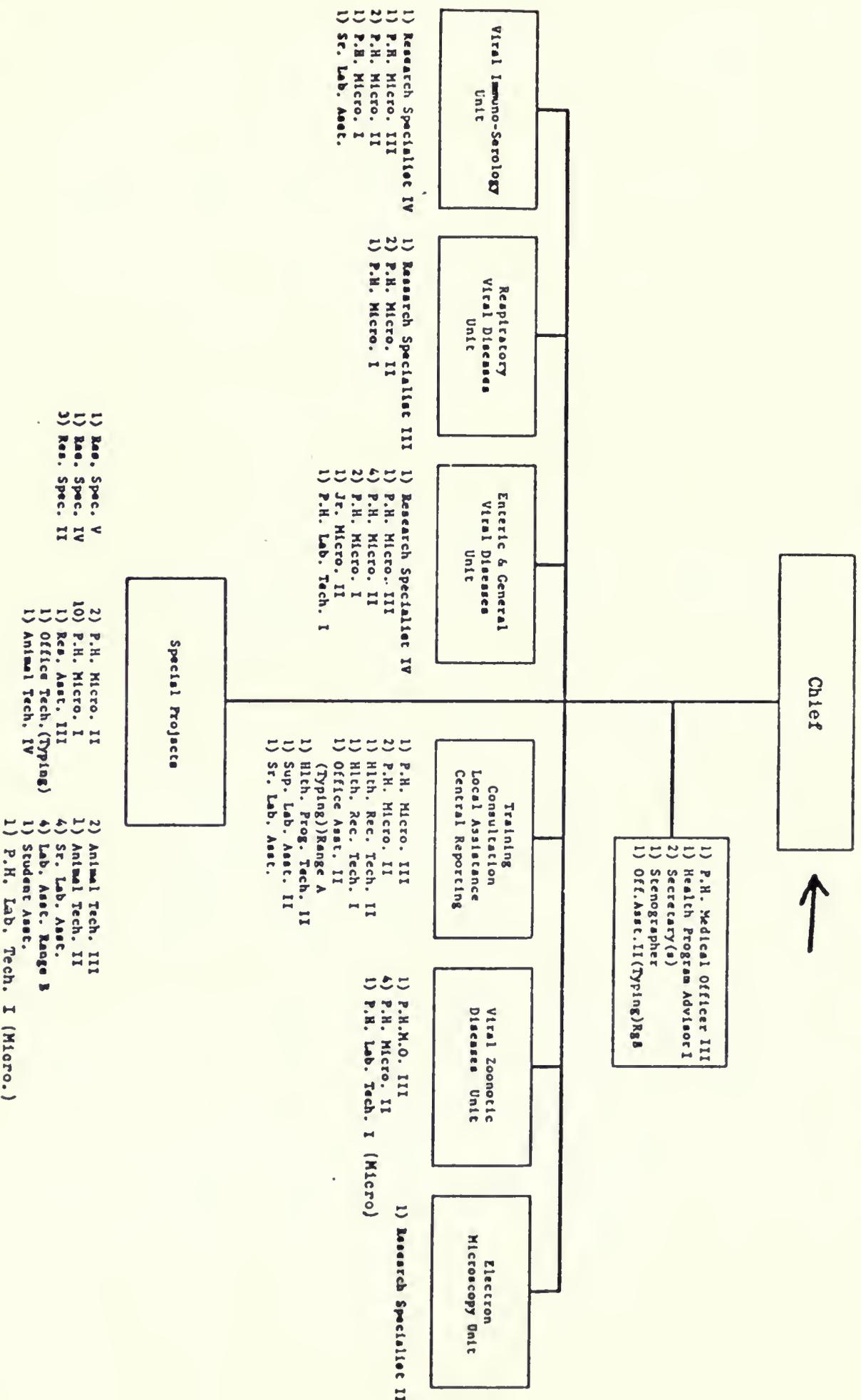
PUBLIC HEALTH DIVISION  
DEPUTY DIRECTOR 8.0



409

5/26/78

Responsible for laboratory support, technical assistance, and research required for diagnosis, investigation and control of viral diseases and for development and maintenance of high quality local viral laboratory services in California.



*Pass Time* 10-9-77

## INDEX -- Edwin H. Lennette

- Abinatti, Francis, 104, 288, 318  
 acquired immunodeficiency syndrome.  
   See AIDS  
 adenoviruses, 71, 136, 138, 142  
   vaccine, 143, 147-149, 198  
   See also specific adenoviruses  
 AIDS, 111-112, 127  
 American Association of Immunologists, 266, 268, 269  
 American Board of Medical Microbiology, 261  
 American Public Health Association, 205, 211  
   Committee on Laboratory Standards and Practices, 211  
 American Society for Microbiology, 99, 210, 258, 261-268  
 American Society for Virology, 263  
 American Type Culture Collection, 178  
 Andrewes, Christopher, 120  
 antibiotics, 45, 97, 112, 113, 238  
   aureomycin, 71, 105, 106-107  
   penicillin, 71, 97, 98, 112, 113  
 antimetabolic agents, 138  
 Armed Forces Epidemiological Board, 198, 225, 269-271  
   Commission on Influenza, 120, 141-142, 147, 158  
   Commission on Rickettsial Diseases, 141  
   Dr. Lennette member, 141-142  
 arthropod-borne viruses (arboviruses), 55, 74, 200, 201, 217, 241, 275  
   See also specific arboviruses  
 Association of California Public Health Laboratory Directors, 254, 317  
 Avery, Oswald, 245-246  
 bacteriophage, 53, 140, 211  
 Balows, Albert, 210, 262  
 Bauer, Johannes, 14, 17, 39, 41, 57, 282  
 Bawden, Frederick C., 64, 243-244  
 Bayne-Jones, Stanhope, 269  
 Beams, Jesse, 281-282  
 Beard, Joseph, 145, 206  
 Beck, Dorothy, 46, 101, 290  
 Bell, Joseph, 290  
 Bell Telephone Laboratories, 231  
 Berg, Gerald, 206  
 Berg, Paul, 249-250  
 Blair, John E., 209  
 Blumberg, Baruch, 192  
 Bodian, David, 24  
 Bodily, Howard, 205-206  
 Bordet, Jules, 43, 249  
 Breslow, Lester, 175  
 Brodie, Maurice, 22, 150  
 Brodzinsky, Phil, 229  
 Bronfenbrenner, Jacques, 33, 39  
 Brown, Edmund G., Jr. (Jerry), 86, 87, 228, 230  
 Brown, Edmund G., Sr. (Pat), 86, 87, 228  
 Brown, Gordon, 158  
 brucellosis, 93, 194  
 Bryan, Earl, 86-87  
 Bucher, Hans, 304  
 Bureau of Biologics, 159, 164, 165, 190  
 Burnet, Frank MacFarlane, 23-24, 80, 101  
 Caldwell virus (echovirus type 31), 133, 135  
 California Department of Health Services. See California State Department of Public Health  
 California Public Health Foundation, 228-232

- California State Board of Health, 86-87
- California State Department of Public Health
- Air and Industrial Hygiene Laboratory, 124, 222
  - Bureau of Chronic Diseases, 175
  - Bureau of Communicable Disease, 88, 94
  - Bureau of Infectious Diseases, 88, 130, 164, 192, 194, 195, 216
  - Bureau of Vector Control, 88, 89, 103
  - construction and design, 82-86, 240
  - Division of Laboratories, 205, 222, 227
  - Division of Research, 164
  - Microbial Diseases Laboratory, 113, 129
  - Preventive Medical Services Division, 229
  - relations with the State of California, 81-82, 86-87, 116, 124-125, 228, 230-231, 234, 242
  - reputation, 87, 124, 227
  - Rockefeller Foundation Laboratories at, 46-47, 68-73, 75-78, 218-219, 220, 225. See also Eaton, Monroe D.
  - Viral and Rickettsial Disease Laboratory (Virus Lab)
    - collaboration with other units and institutions, 88-89
    - construction and design, 56-57, 116-117, 176-177
    - funding, 114-115, 218-227, 231
    - public health orientation, 121
    - reputation, 240-242, 287
    - research. See specific diseases
    - staff, 316-319
    - and the State of California, 114-116, 176-177, 219-222, 225, 227, 243, 310
    - training programs, 124, 129-130, 232-237, 287, 317
    - viral diagnosis, 115, 125-127, 215-221, 311
- California virus, 89, 93
- Camp Detrick, Maryland, 74, 83, 84, 85, 89
- Campbell, Daniel, 178
- cancer
  - causes, 278, 293
  - research at the Virus Lab, 172, 175-183, 204, 293, 298, 310
  - research, phases in, 182-183
- Cannon, Paul, 20
- Casals, Jordi, 56, 294
- cell culture. See tissue culture
- Center for Disease Control, 85, 167, 187, 207, 296
- Dr. Lennette consultant, 273-274
- funding of Virus Lab, 225, 241
  - lecture and laboratory courses, 125, 234, 236-237
- Chanock, Robert M., 70, 143, 292
- chicken leukemia virus, 206
- Chin, James, 130, 197-199
- China Medical Board, 25
- Chumakov, Mikail, 169-170
- Clark, Paul F., 14
- Clark, William, 103, 229, 288, 290
- Coe virus (coxsackie A21), 133, 142, 145, 241
- Coggeshall, Lowell T., 40, 46
- Collen, Morris F., 69n
- Coons, Albert, 118
- Congo virus/fever, 275
- conjunctivitis, acute hemorrhagic, 136, 241
- Connaught Laboratories, 163
- Coriell, Louis, 260
- Cornell, Channing, 307
- Cox, Herald, 38, 101, 106, 168, 284
- Coxiella burneti, 101
- coxsackie viruses, 67, 131, 135, 136, 195, 198
- See also specific coxsackie viruses
- Crawford, Robert, 11
- Cremer, Natalie, 130, 178, 204
- Cutter Laboratories, 133, 159-167
- cytomegalovirus, 27-28, 35-36, 127, 189, 207-208

- Dack, Gail Monroe, 10-11, 12, 15  
 Dalldorf, Gilbert, 67, 135  
 Davis, Dorland J., 186  
 Dean, Ben, 101  
 de Kruif, Paul, 21  
 Derrick, E. H., 100, 106, 292  
Diagnostic Procedures for Bacterial,  
 Mycotic and Parasitic  
 Infections, 213  
Diagnostic Procedures for Viral and  
 Rickettsial Infections, 99,  
 211-212, 213, 220  
 diarrhea, infant, 139  
 Dingle, John, 270  
 DNA, 245  
   recombinant, 85, 136, 167, 177,  
   249-254  
 Drew, Lawrence, 128  
 Dubos, Rene, 40  
 Dulbecco, Renato, 139-140  
 Dyar, Robert, 164, 228
- East African Virus Research  
 Institute, 275, 277  
 Eaton, Monroe D., 39-40, 44, 46,  
 75, 141  
   research on the Eaton agent,  
   68-71  
   at the Rockefeller Foundation  
   Laboratories, Berkeley, 78,  
   79, 91, 215, 218, 317  
 ECHO viruses, 295  
 Eddie, Bernice, 90  
 Ehrlich, Paul, 184  
 electron microscopy in virology,  
 64, 196-197, 206, 244  
 electrophoresis in virology,  
 244-245, 283  
 Emmons, Richard, 240  
 encephalitis  
   arthropod-borne, 55-56, 200, 201  
   Dr. Lennette's research in St.  
   Louis, 36-37, 73  
   early research in California,  
   91-93  
   Hooper Foundation research, 89-90  
   research in Brazil, 54-56, 58, 60  
   encephalitis (continued)  
     research supported by National  
     Foundation for Infantile  
     Paralysis, 155  
     research at Virus Lab, 71-73,  
     79, 88, 131, 219, 242  
 Enders, John, 301  
   and Salk vaccine field trials,  
   159, 161, 165  
   tissue culture methods, 23, 117,  
   126, 149, 151, 152, 157, 258,  
   318  
 endocarditis, 106  
 England, Beatrice, 318  
 enteroviruses, 131, 132, 133,  
 136, 137, 241  
   identification of, 134-135  
   nonpolio, 130-133  
     See also ECHO and coxsackie  
     viruses  
 Environmental Protection Agency,  
 182  
 Epstein-Barr virus, 316
- Fayinka, O. A. (Tunji), 276  
 Federation of American Societies  
 for Experimental Biology,  
 268-269  
 Federov, Sergei, 260  
 Findlay, George M., 66  
 Flexner, Simon, 28-29, 224  
 Flossdorf, Earl, 309  
 Flow Laboratories, 301-302  
 Fogerty, James, 184, 185  
 Food and Drug Administration, 47,  
 159, 290, 304, 305-306, 308,  
 309  
 food poisoning, 12-13, 58  
 Fox, John, 20, 54, 63, 121, 122,  
 168  
 Francis, Thomas, 46, 100, 197,  
 211, 256, 263-264, 272  
   Armed Forces Epidemiological  
   Board, 141, 270  
   influenza, 44, 45, 119-120, 141,  
   144, 193, 285  
   poliomyelitis, 158, 160, 166

- Franklin, Opal, 106  
 Franklin, Rosalind, 246  
 Freeman, J. M., 203  
 Friedman, Harvey, 124  
 Fujimoto, Frances, 318
- Gajdusek, Carlton, 186  
 Gard, Sven, 161  
 Gardner, Murray, 310  
 Gassler, Viktor, 303, 304, 307, 308  
 gastroenteritis, 136  
 Georgia Warm Springs, 200  
 Gerhardt, Phil, 261-262  
Giardia lamblia, 207  
 Goodner, Kenneth, 44-45  
 Gordon, Francis, 18, 23-24  
 Gordon, Robert, 195  
 Griffith, Frederick, 245
- Halvorson, Harlan, 75, 153, 155, 156, 262, 298  
 Hammon, William McDowell, 90, 91, 92, 154, 240, 262  
 hand and mouth disease, 195, 218  
 Hansler, William J., Jr., 210  
 Harding, Harry, 295  
 Harper, William Rainey, 7  
 Harris, Jean, 318  
 Harrison, James, 18  
 HeLa cell line, 258-259  
 Henle, Gertrude (Brigitta), 123, 316  
 Henle, Werner, 123, 284, 316  
 hepatitis, 49, 122, 193  
   diagnosis, 127, 188, 189  
   research at Virus Lab, 73, 110, 192, 219, 296  
 Herndon, R. M., 203  
 herpes, 111, 127, 132, 173, 188, 189, 242  
 Hermann, Kenneth, 296  
 Hill, Lester, 184, 185  
 Hilleman, Maurice, 143, 279-280  
 Ho, Helen, 318  
 Hollister, A. C., 164  
 Holmes, Monroe, 104  
 hookworm disease, 39
- Hooper Foundation, 88, 89-91, 197  
   See also Meyer, Karl F.  
 Horsfall, Frank, 54, 70, 283  
   Dr. Lennette's influenza research with, 39, 41, 42, 43-44, 45-46, 48, 50, 193  
 Horstman, Dorothy, 296  
 Howitt, Beatrice, 90-91  
 Huang, C. H., 71, 72, 117, 156-157  
 Huebner, Robert J., 174, 264  
   cancer, 145, 179-180, 204, 225, 277, 293, 310  
   Q fever research, 78, 101-103, 104, 106, 241, 288, 290, 291  
 Hudson, Noel Paul, 34  
   Dr. Lennette's research with, 18, 19-20, 22, 24, 25, 26, 31, 32  
   yellow fever research, 14, 15-17, 27, 57, 248  
 Hummeler, Klaus, 123  
 Huntington, Robert, 40
- infectious disease physicians, 97-98, 113, 215  
 influenza, 119, 123, 144-145  
   research at Fort Ord, 142-149  
   research at the Rockefeller Institute, 39, 41-42, 45-46, 47-50, 54, 68, 120, 122  
   research at the Rockefeller Laboratories, Berkeley, 76, 141, 215  
   research at the University of Michigan, 119-120  
   vaccines, 43, 47-48, 81, 88, 142, 145, 146, 198, 285  
   virus nomenclature, 48-49, 50, 143, 146, 193  
 Institut Virion AG, 290, 296, 300  
 International Congress on Virology, 137  
 International Committee on Taxonomy of Viruses, 137  
 Isaacs, J., 66

- Jellison, William, 290  
 Jensen, Florence, 318  
 Johnson, Harald Norlin, 200-203, 225, 295  
 Jones, W. Alton, Cell Science Center, 259-261  
 Jones, W. Alton, family, 259-261  
 Jordan, Edwin Oakes, 11  
Journal of Clinical Microbiology, 308  
Journal of General Virology, 265, 266  
Journal of Immunology, 266  
Journal of Virology, 264-265  
 Jung, Mirko, 307  
 Jungeblut, Claus W., 14, 117, 156
- Kapikian, Albert, 136  
 Kaplan, Martin, 274  
 Kerr, Austin, 55, 63  
 Kessel, John, 24  
 Kinyoun, Joseph, 184  
 Kneeland, Y., Jr., 120  
 Knight, Arthur, 80  
 Koch, Robert, 184  
 Kolmer, John, 23, 150  
 Kono, Reisaku, 136  
 Koprowski, Hilary  
   development of a live polio vaccine, 168  
   research by Dr. Lennette and, 65, 66-67  
   research on subacute sclerosing panencephalitis, 202-204  
   research on yellow fever, 55, 63-64  
 Kossobudzki, Luty, 60, 63  
 Kumm, Henry, 154, 155
- Laboratory Diagnosis of Viral Infections, 98-99, 213  
Laboratory Procedures for the Diagnosis of Viral, Rickettsial and Chlamydial Infections, 99-100
- Laemert, Hugo, 61-62  
 Lancz, Gerald, 300  
 Landsteiner, Karl, 266  
 Leach, John, 200, 200n  
 Lederle Laboratories, 106, 168, 280  
 Lennette, David Alan (son), 315-316  
 Lennette, Edwin H.  
   administrative duties at the Virus Lab, 254-255, 297-299  
   consultancies and memberships in professional associations, 256-279  
   doctoral dissertation, 22  
   editorial contributions, 98-100, 209-215  
   family background and education, 1-13, 313-315  
   research  
     in Brazil, 54-62  
     at Camp Detrick, 74  
     at Fort Ord, 142-149  
     at Washington University School of Medicine, 33-37  
     See also specific diseases  
   teaching at the University of California School of Public Health, 239-240  
   thoughts on graduate, public health, and medical education, 112, 128-129, 237-238, 249  
 Lennette, Edwin Paul (son), 315  
 Lennette, Elizabeth (wife), 314-315  
 Lennette, Evelyne Tam (daughter-in-law), 315-316  
 Leonards, Richard, 242  
 Lerner, Richard, 253  
 Levy, Jay, 316  
 Lindenmann, J., 66  
 Loosli, Clayton, 145, 186  
 Luoto, Lauri, 101  
 Lyman, Donald, 229  
 lymphocytic choriomeningitis virus, 47, 132

- MacCallum, F. O., 66  
 McCarty, Maclyn, 245-246  
 McCordock, Howard, 33, 34, 35  
 McGarrity, Gerard, 258  
 McKinley, Earl Baldwin, 13  
 MacLeod, Colin, 160, 245-246,  
 270, 272  
 Maggs, Marjorie, 318  
 Magill, Thomas P., 44, 48, 120  
 Magoffin, Robert L., 77, 130,  
 193-195, 203, 220, 254  
 malaria, 39, 40, 46, 193  
Manual of Clinical Microbiology,  
 99, 209-210, 212  
 Margulis, Lynn, 248, 294  
 Marin agent, 136  
 Markham, Floyd, 18n, 28  
 Marmion, Barry, 70  
 Martins, Mary, 317  
 Mayer, Manfred, 173, 295  
 Maza, Luis de la, 300  
 MediCal, 86, 232  
 Meiklejohn, Gordon, 69, 106,  
 107, 141, 142, 219  
 Melnick, Joseph L., 25, 136,  
 137, 206, 264  
 Merchant, Donald, 260  
 Merck, Sharpe and Dohme Company,  
 Inc., 162, 163, 167, 279,  
 280  
 Merrill, Malcolm, 75, 81, 164,  
 226, 228, 298  
 Metcalf, Theodore, 206  
 Metchnikoff, Elie, 31  
 Meyer, Karl F., 14-15, 89-91,  
 92, 109, 159, 197  
 Meyers, Beverly, 229  
 Meyers, Harry, 190  
 microbiology, 85-86, 96  
 Milbank Fund, 19, 21, 28  
 Mirick, Richard, 70  
 Modoc virus, 201  
 molecular biology/virology,  
 49, 53, 95, 96, 112, 122,  
 123, 210, 211  
 Moloney leukemia virus, 204  
 mononucleosis, 146  
 Monroe, Vincent, 260  
 Moore, Robert, 35  
 Morgan, Councilman, 196  
 Morrison, Robert, 201  
 Mosiman, Josephine, 308  
 Muckenfuss, Ralph, 90, 122  
 mumps, 123, 131, 132  
 virus, 146, 195, 241  
 Nakamura, Koichi, 318  
 National Advisory Allergy and  
 Infectious Diseases Council,  
 185-186  
 National Cancer Act, 183, 277  
 National Cancer Institute, 175,  
 176, 179-182, 225, 277  
 National Foundation for Infantile  
 Paralysis, 131  
 funding of polio research, 21-  
 22, 24, 130  
 gamma globulin prophylaxis, 154  
 Salk vaccine field trials, 158,  
 168, 170, 285, 296  
 support of nonpolio virus  
 research, 155  
 support of polio research at the  
 Virus Lab, 132, 153, 173, 295  
 National Institute for Neurologi-  
 cal Diseases, 186  
 National Institute of Allergy and  
 Infectious Disease, 70, 101,  
 180, 186, 225, 278, 279  
 National Institutes of Health,  
 36, 159, 241, 292-293  
 evolution, 184-186  
 study sections, 223-225, 298-  
 299  
 Neff, Beverly Jean, 318  
 Neva, Frank, 187  
 New York City Public Health  
 Research Institute, 54, 121-  
 123, 284  
 Nieman, Irving, 18  
 Nigg, Clara, 41-42, 119  
 Nixon, Richard, 183  
 Noguchi, Hideyo, 15, 16  
 Norwalk agent, 136  
 nosocomial infections, 95-96

- O'Connor, Basil, 21, 154, 155, 156, 170
- Olitsky, Peter, 37, 38, 56, 284
- oncogenes, 103, 180
- ornithosis, 90
- Oshiro, Lyndon, 196-197, 202
- Ota, Margaret, 318
- Pait, Charles, 24
- Pan American Group for Rapid Viral Diagnosis, 302  
award to Dr. Lennette, 312
- panencephalitis, subacute sclerosing, 202
- parainfluenza virus, 148, 203
- Parke-Davis and Company, 133, 162, 280
- Parkinan, Paul, 190
- Parkman, Paul, 187
- Paul, John, 110, 185, 223, 298
- Penna, Enrique, 58, 62
- Perlowagora, Elena, 55, 64
- Pickels, Edward C., 122, 281-283
- Pirie, Norman W., 64, 243-244
- pleurodynia, epidemic, 195
- Plotkin, Stanley A., 124
- pneumonia  
antiserum, 45  
atypical, 68-71, 118, 198, 215
- poliomyelitis  
cultivation of virus, 152  
Cutter vaccine episode, 159-167  
diagnostic tests, 117, 131, 173, 174, 217, 271, 294  
early vaccines, 22-23, 150  
gamma globulin prophylaxis, 154-155  
immunity, 30-31  
nonparalytic, 119, 130, 131, 156, 294  
portal of virus entry, 28-30  
research at the University of Chicago, 20-31  
research at the Virus Laboratory, 130-133, 153-167, 171-175, 195, 294-296, 298  
Sabin vaccine, 132, 163, 166, 168-171, 285
- poliomyelitis (continued)  
Salk vaccine, 120, 132-133, 153, 154, 155-167, 168, 169, 285, 296
- Price virus, 133
- prostaglandins, 246
- rabies, 76, 200, 318
- Railsback, Oscar, 292
- Randall, Judy, 189
- Rasmussen, Frederick, 262
- Reeves, William, 89, 91, 92, 93
- reoviruses, 137-141
- respiratory diseases/viruses, 76, 120  
Fort Ord studies, 88, 142-146, 197-199  
See also specific diseases/viruses
- respiratory syncytial virus, 148, 190
- rhinoviruses, 198
- Rhodes, Andrew J., 17, 52
- Rickard, Elsmere R., 41, 42, 49-50, 58, 119
- rickettsialpox, 103, 291
- Riggs, John, 178, 197, 205, 207
- Rivers, Thomas, 14, 18, 38, 51, 160, 286  
books by or about, 13, 16, 247  
Dr. Lennette's associations with, 33, 34
- Robbins, Frederick C., 126, 149, 151, 152, 258
- Robin, Yves, 275
- Rockefeller Foundation, 25, 50, 56, 57, 59  
International Health Division, 14, 37-41, 44, 45, 50, 65, 68, 70, 122, 201  
laboratory in Budapest, 41  
laboratory in Entebbe, 275  
laboratory in Poona, 200  
laboratories in Berkeley. See California State Department of Public Health
- Rockefeller Institute for Medical Research, 50, 53, 224
- Rockefeller, John D., 7
- Rockefeller University, 224

- Romer, Mary, 104, 106, 288  
 Roosevelt, Franklin D., 21, 22, 185, 223, 224  
 rotaviruses, 136, 139  
 Rothamsted Experimental Station, 64  
 Rous, Peyton, 182  
 Rous sarcoma virus, 182  
 Roux, Emile, 184  
 Rowe, Wallace P., 181  
 rubella, 186-190, 274, 296  
   cultivation of virus, 297  
 rubeola, 198  
   virus, 202, 203  
 Rush Medical College, 8  
 Russell, William, 303
- Q fever  
   research in southern California, 78, 100-106, 288, 290-291  
   research at the Virus Lab, 79, 81, 93, 103-109, 121, 141, 226, 241, 274, 288-293, 298, 311
- Sabin, Albert, 38, 284-286, 295, 301  
   polio research, 28, 37 See also  
   poliomyelitis  
   polio vaccine, 132, 168, 169, 170 See also poliomyelitis  
 Sabin polio vaccine. See poliomyelitis  
 Sadusk, Joseph, 173  
 Salk Institute for Biological Studies, 163, 170-171  
 Salk, Jonas, 284-286  
   influenza research, 44, 120, 147, 285  
   metabolic inhibition test, 173  
   polio research, 24, 117, 156, 285 See also poliomyelitis  
   polio vaccine, 23, 156, 160, 161, 165, 168, 169 See also poliomyelitis  
 Salk polio vaccine. See poliomyelitis  
 Sawyer, Wilbur A., 39, 40, 41, 121-122, 219  
 Schachter, Julius, 109  
 Scharrer, Ernst and Berta, 246  
 Scheele, Leonard, 163, 164, 165  
 Scheiss, Peter, 304, 307  
 Schieble, Jack, 130, 197-199  
 Schmidt, Leon, 486  
 Schmidt, Nathalie, 130, 135, 192, 194, 209, 254, 294-297, 301  
   complement fixation test, 117, 151, 295  
   editorial efforts, 100, 211  
   intersecting serum scheme, 131, 134  
   polio research, 172-174  
   rubella research, 186, 187  
 Schultz, Edwin Weston, 14, 29, 91  
 Seal, John, 145  
 Selas, Michael, 253  
 Seto, Gordon, 260  
 Shadomy, H. Jean, 210  
 Shannon, James, 184, 185, 223, 272, 273  
 Shearer, Lois Ann, 198  
 Shephard, Charles, 78, 101, 288  
 Shimkin, Michael, 182, 183  
 Shinomoto, Tak, 318  
 Shon, Carol, 71, 72, 73, 318  
 Siegal, Michael, 123  
 "slow virus" infections, 186  
 Smadel, Joseph, 34, 100, 160, 211, 256, 264, 272, 280, 301  
   viral diagnostic laboratory, 68  
   viral electrophoresis, 244, 245  
 Smith, Charles Edward, 83, 239  
 Smith, Hugh, 70  
 Smith, Margaret, 35-36, 207-208  
 Sohler, R., 136  
 Soper, Frederick, 57, 59, 61, 62, 63n  
 Spaulding, Earl, 210  
 Specter, Stephen, 300  
 Spendlove, Rex, 137-141, 196  
 Spink, Wesley, 194  
 Stanley, Wendell, 161, 243-244  
   virus biochemistry, 51, 52-53, 80, 245  
   Virus Laboratory, University of California, Berkeley, 79, 80-82, 196  
Stedman's Medical Dictionary, 98  
 Sternberg, George M., 43

- Stokes, Edwin Westin, 14, 29, 91  
 Stritar, Joseph, 18n  
 Strode, George, 122  
 Swift, Homer, 43, 284  
 syphilis  
   Kolmer test, 150  
   serology, 122  
 Syverton, Jerome, 38, 256, 258, 284
- Taylor, Richard Moreland, 41, 49  
 tenBroeck, Carl, 81  
 ter Meulen, Volkner, 203  
 Theiler, Max, 28-29, 40, 54, 57  
 Thompson, Barbara, 318  
 tissue/cell culture, 71, 117, 126-127, 134, 146, 149, 151-153, 157, 173, 256, 258  
 Tissue Culture Association, 256-259, 260, 261  
 Toomey, John, 29-30  
 Trask, James, 223  
 Truant, Joseph P., 209  
 tuberculosis, 95  
 Turlock virus, 88, 93, 241
- ultracentrifuge, 244, 281-282  
 United States-Japan Cooperative Medical Science Program, 271-273  
 University of California  
   Donner Laboratory, 81  
   Medical Center, San Francisco, 88, 109  
   School of Public Health, Berkeley, 83, 89, 91, 93, 186, 226-227, 239-240
- van Allen, Alwine, 317  
 Van Rooyen, Clennel E., 17-18, 52  
 varicella, 209, 296  
 Verder, Beth, 11-12  
 Viral and Rickettsial Disease Laboratory (Virus Lab). See California State Department of Public Health
- viral diagnosis, 76-78, 127-128, 279, 280  
   future of, 128-130  
   kits, 188-189, 208, 214, 281  
   laboratories, 68, 76, 119-124  
   rapid, 190-191, 302, 311  
   training programs in, 113-114, 125, 232-237  
   at Virus Lab. See California State Department of Public Health
- viral diagnostic tests/methods  
   complement fixation, 43, 44, 73, 117, 131, 151, 173, 174, 219, 284, 295, 305  
   hemagglutination inhibition, 43-44, 118, 187, 219, 283-284, 296  
   immunoenzymatic, 118, 191, 216  
   immunofluorescence, 134, 178, 190, 191, 208, 216, 233, 318  
   metabolic inhibition, 117, 118, 131, 151, 152-153, 173, 174  
   neutralization, 42-43, 44, 67, 73, 117, 150, 151, 152, 157  
   passive hemagglutination, 118  
   plaque, 139-140  
   radioimmunoassays, 118, 191, 216  
 Virion, Inc., 290, 296, 300  
 Virolab, Inc., 316  
 virology  
   instruction in the 1930s, 13-15, 17  
   training, 94-98, 110-111  
   use of embryonated egg, 69, 100  
   use of suckling mice, 66-67  
   water, 205-207  
   See also viral diagnosis, viral diagnostic tests/methods, viruses  
Virology, (journal), 265-266  
 Virus Laboratory, University of California, Berkeley, 79, 80-82, 196
- viruses  
   crystallization, 80, 243-244  
   identification, classification, and naming, 133-137, 146  
   interference, 65-66, 190

- viruses (continued)  
 lyophilization, 309  
 nature, 17, 51-52, 243-248,  
 293  
 von Behring, Emil, 184  
 von Magnus, Herdis, 161  
 von Magnus, Prebend, 135
- Ward, Paul, 232  
 Warren, Earl, 86, 221  
 Warren, Joel, 301, 303  
 water virology, 205-207  
 Watson, Dennis, 178  
 Watson, James, 251  
 Webster, Robert, 228  
 Weiner, Anna, 152, 318  
 Weisner, Jerome, 272  
 Welch, Hartwell, 101, 103, 288,  
 290  
 Wellcome Trust, 275  
 Weller, Thomas H., 126, 149,  
 151, 152, 187, 209, 258  
 Wenner, Herbert, 135  
 Whitely, Helen, 262  
 Wickman, Ivar, 29  
 Williams, Robley, 196-197  
 Wilson, Luke, 184  
 Winn, John, 101, 104, 290  
 Woodie, James, 318  
 Woodland Clinic, 105  
 Woods, Willis, 262  
 Woolpert, Oram, 18  
 World Health Organization, 144,  
 146, 228, 234  
 Dr. Lennette's work with,  
 142, 143, 236, 274-277
- Yamamoto, Sachiko, 318-319  
 yellow fever  
 research in Africa, 14, 26, 57  
 research at the Rockefeller  
 Institute, 39  
 research in South America, 54-  
 62, 154  
 research at the University of  
 Chicago, 15-17  
 vaccine, 28, 39, 40, 45, 54,  
 58, 68, 171
- Yellow Fever Service, 59, 60,  
 61, 62, 63  
 Young, Frank, 100, 101
- Ziedins, Inta, 318

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