This is Dr. Olch of the National Library of Medicine, visiting in the office of Dr. Donald Dexter Van Slyke at Brookhaven National Laboratories. The date is May 27, 1969. We are going to begin most informally, discussing Dr. Van Slyke's childhood and early education. I do know, and that's about the limit of it, sir, that you were born in Pike, New York.

Dr. V.: That's right. At the time of my birth, my father was an instructor in chemistry at the University of Michigan. It happened that my mother was staying with his parents in the town of Pike when I arrived on the scene. I don't know why it was particularly convenient for her to be there, but that was the way it happened. So my birthplace was Pike, New York. The old name was Pike Hollow because it was in the valley between two rather high hills. It was a village of a few hundred people on one of the main wagon roads between Buffalo and New York, and was rather active in early days. It had saloons where drivers would get comfortably drunk. It had a small river which was used for water power to run a woolen mill and a gristmill, and provided a millpond which was good for swimming.

Dr. O.: You were born there, but did you actually live there awhile? You sound as though you spent a fair amount of time there in your childhood.

Dr. V.: Later I went back when I was about five years old. I went, of course, with my parents to Ann Arbor and was there until I was two years old, then my mother died of puerperal fever when a younger brother was born. There were no antibiotics to prevent that sort of thing then. My father went to the Hawaiian Islands as Professor of Chemistry in the Punaha School in Honolulu, and left me with an older sister of his who lived on a farm only three miles from the town of Pike where I was born. So I had those early years 'till I was about six years old in the country and I remember it very, very vividly. As a matter of fact, I went back and spent part of my vacations there with my aunt every year until after I got through college. So I grew up knowing what farm life is.

Dr. O.: Your father did later move to New York State, did he not?

Dr. V.: Yes, he came back after three years in Hawaii. At the end of that time, he married again and came back and took a position again on the faculty at Ann Arbor. So I had a year in Ann Arbor when I was about six years old. I still remember that. I got a very bad impression of girl medical students at that time.

Dr. O.: At the age of six! Most of us, if I may be so bold, have to wait awhile-----

Dr. V.: (Laughter) Which I have overcome completely, but it happened this way. Living on the farm, the animals were individuals to me. They all had names and they were all friends, and in particular we had what was called a coon cat. That's a very large cat with yellow and white tiger stripes. Very unusual. You don't see them very often, but they're large and they are very intelligent. This cat would go out with me to get the cows, and come back. I missed the animals when we went to Ann Arbor, but after a little while I noticed that there was a duplicate of this cat at the house next door and I made friends with him and was very happy. Well, there was a girl medical student living in the same house where we lived. I became friendly with her and introduced her to this cat, whose name was "Harry." In the Medical School at that time, there was a janitor who was an old pirate, and all the children in Ann Arbor knew that if he could catch you they'd take you in and dissect you! So it was a great game to start running when you came by the Medical School and run until you got past! Well, this girl medical student suggested that I introduce her to "Harry," so one day I brought him over and gave him a proper introduction and she gave me a nickel to go out and buy a bag of peanuts. When I came back I saw the most horrible sight that ever came into my life and I haven't forgotten it yet. This old pirate was there with a big sack and "Harry" was being poured into it, head first, to be taken over and dissected! And I begged that "Harry" be released but this medical student was adamant. All she had to say was she was sorry I got back so soon! If I saw her today I would hate her! But afterwards, I met other girl medical students that taught me that she was not a fair sample!

Well, we were one year in Ann Arbor and then my father went to the Johns Hopkins to do some postgraduate work with Ira Remsen, and during that year I went back to live with my uncle and aunt on a farm which was three miles from Pike, so I got in contact with Pike again. Then father became chemist at the New York State Experiment Station at Geneva.

Dr. O.: That's what I was thinking of previously.

Dr. V.: So I joined him again and grew up in Geneva, which was a delightful town. It had a very good high school with excellent teachers. There were no junior disturbances in those days!

Dr. O.: Were there any particular teachers in high school you think that had any major role in your education?

Dr. V.: Yes there were. There were two. They were both women and they were both elderly women. One of them was Miss Hancock who was in charge of the boys. There were 100 boys in high school and when they were not reciting in the side rooms they were all there together under her supervision and she kept perfect order in that room. She was a powerful and benign personality. She knew all of those boys. If there was anything that happened that was out of order she would know what was going on immediately and it would be corrected. Once in awhile whe would call a boy up and have a nice little talk with him about something that she thought would be profitable to him. Occasionally she would talk about things that were not mathematics--she taught mathematics. I remember particularly once she spoke about the nude in art, and she said the entire body expresses moods and feelings. And she spoke about a nude that expressed depression and how, as a matter of fact, the bend in the foot seemed to express it more than any other part. She spoke about this famous statue of Laacoan and his two sons, and she said the agony was expressed there in the intensity of the abdominal muscles.

Dr. O.: Sort of a remarkable insight being expressed to a group of high school students, isn't it?

Dr. V.: Yes. She had a nice sense of humor. There was one boy that had a good head but he was lazy and in algebra when we had a hard lesson he was likely to be home sick. One day we came to a rather hard part and he didn't show up. The next day he did show up and she said, "Well, Vrooman (he came from an old Dutch family, Vrooman), how did you get on with the lesson yesterday?" "Yes," he said, "I've done all those problems!" and he had them all worked out. And she said, "Vrooman, if we meet twenty years from now, we'll have something to talk about!" (Laughter)

The other teacher was a Miss Florence Parker. She had a similar, you might call it administrative, position in charge of the girls side of the high school--but she taught English and she was better than any English teacher I had in college. She taught the rules of grammar and how the English sentence was formed and how you should express yourself in a way that would be clear to the particular people who would read what you were writing. I think the fact that I have been considered a fairly lucid writer in scientific work has been to a very large extent due to what Miss Parker taught me. She eventually retired and I went back to see her every year when I'd be back in Geneva--I'd go back to visit my stepmother. When Miss Parker was ninety there was a great celebration in Geneva and she had greetings from a great many important people, I think including the President. She lived to be 103! I saw her every year until the year she died. She was a very fine teacher. She had both the technique and the feeling.

Dr. O.: Did they influence you, sir, in a sense that they convinced you or were important in your decision to go further in your education into college, or specifically toward the sciences?

Dr. V.: No, no. I always took it for granted that I would go to college. I didn't know when I went to college whether I would go into architecture or chemistry. I was always interested in architecture but after my first year in college I decided on chemistry.

Dr. O.: Had you had any chemistry in high school? Was there any sort of a physical science course in high school?

Dr. V.: No. I had had physics in high school but not chemistry. My first year at college I went to Hobart College which is in Geneva--an excellent small college, I enjoyed it very much. I made the varsity football team there which I wouldn't have done in a big university! And I knew every man in college practically. I loved the small college, but it only had one year of chemistry so I couldn't stay longer than that. Then I went to Ann Arbor. Although it was my father's college, the chief reason I went there was that Moses Gomberg was there. If there was any outstanding American organic chemist, it was he. I went on my father's advice and had his help in planning my course of study at Ann Arbor. As a matter of fact, he went out with me when I went there; he knew the faculty. We went around and saw the professors of chemistry and laid out a definite plan of organic and physical and analytical chemistry which was a great advantage.

Dr. O.: I'm sure this was.

Dr. V.: I expected to go into agricultural chemistry which was my father's line. He was sort of the Dean of Agricultural Chemists in his day. He was thirty-nine years in the Geneva Agricultural Experiment Station.

Dr. O.: He also had received his training in chemistry at Ann Arbor, is this right?

Dr. V.: Yes. So besides chemistry I took bacteriology and plant physiology as minors for my doctor's degree. I stayed on in Ann Arbor after I took my bachelor's degree and took my doctor's degree also there. Then I took a competitive examination for a position in Washington in the Bureau of Chemistry and won it and was enrolled among the government employees and expected to go there right after commencement in 1907. It happened at the spring meeting of the American Chemical Society that year, my father sat next to P. A. Levene who was chemist at the newly started Rockefeller Institute. They got to talking about how there was so much more demand for well-trained chemists than there were available for research work and my father mentioned the fact that I was taking my degree at Michigan that time and there were various positions I could have had and Levene asked if I'd be interested in coming to the Rockefeller. As a result, I got a letter from Dr. Flexner, who was the head of the Institute, inviting me to come to New York for an interview. Well, the Rockefeller Institute had just gotten started, it didn't amount to anything and the government was a big thing. I didn't have the slightest idea of taking a job with the Rockefeller and giving up the government one, but here was a chance for a trip to New York with expenses paid! (Laughter)

Dr. O.: Little did you know!

Dr. V.: And so I went down and it happened Levene was away at the time, but I had a long talk with Flexner and he told me what was the probable future of the Institute. On the way back to Ann Arbor I stopped at Geneva and talked it over with my father and the result of it was that I resigned the job with the government before I ever went there and took the position with Levene. So that shifted my general field insofar as it was applied chemistry from agricultural chemistry to medical chemistry. I worked with Levene for seven years--worked in his department, worked on proteins and amino acids, and it was a marvelous time working with Levene. He arranged for me to go over, in 1911, to Berlin to work for a year with Emil Fischer who was the great "sun and god" of organic chemistry as long as he lived. There was no doubt that Emil Fischer was the number one man of that world. I had a chance to see how he worked. He got interested at one time in the problem he gave me and had me go into his private laboratory and work right beside him for three or four days.

Dr. O.: For heaven's sakes. This was quite an honor in those days, I'm sure, because a professor's private laboratory was generally off-bounds for the fellows.

Dr. V.: Oh, very much. Everything he did was in a quantitative way. That is, if he were going to do the solubility on a new compound, instead of just putting some of it into a test tube with ether or chloroform or whatever it was to see whether it dissolved or not, he'd take so many milligrams of it and mix it with so many ccs., he'd have an approximately quantitative idea of how soluble it was. I had an uncomfortable five minutes once when I was with Fischer. I was making a compound that required the use of bomb tubes--they're glass tubes, heavy glass tubes that you seal with the substance that you want to heat up under pressure. Then you put it into a bomb furnace--it's an iron furnace with iron tubes that will take this bomb tube and it's so strong that if your bomb tube blows up it will be contained. You heat things up way above the boiling points of whatever liquids you use. Well, I was using these bomb tubes to make a compound that we were using for the work that I was starting.

Dr. O.: These are spelled bomb, b-o-m-b?

Dr. V.: B-o-m-b, yes. The First Chemical Institute (it was designed by Fischer) had a room for bomb tubes and other things that were likely to blow up. There was one particular bomb furnace that was unique. It had crude mineral oil in it that was a mixture of kerosene, gasoline and heavy oil, just as you get it, that boiled up around the chamber that held these tubes. There was a reflex condenser up above and it was arranged so that you started burners under this thing and arranged your reflex condenser so that the gasoline and kerosene and so forth that boiled up into it would be discarded until you got to the boiling point you wanted and then you fixed it so that the condensate would be returned and the mixture continue boiling at that point, so you could set the furnace for any temperature up to maybe 200 centigrade. I was using that. There were three burners and one of them would keep it going at the right temperature and not too rapidly to prevent all of it getting condensed. The condenser was only about a foot long. One morning I went down and put the tubes in and started all three burners in order to get it warmed quickly, intending to go down after five minutes and turn two of them off because the three of them would start pouring gasoline vapor into the air. I returned to the main laboratory, intending to stay there only for a moment before going back to the bomb room to turn off two burners. When I got up to my desk, Fischer came in and came straight to me and started talking. Ordinarily he never came in in the morning. He always took a nap after lunch and came in about two o'clock in the afternoon, but this morning he came right in. And I stood there and was as short as I could be in my answers, but you didn't tell "Excellenz" Fischer, "I've got to hurry; you come back some other time!" (Laughter) I stood there wondering whether the building was going to blow up or what the devil I would do, and finally he said, "Ja!" and he walked off. I went down and opened the door of the bomb room. That room was so full of black soot that I couldn't see the windows on the other side! The gasoline had boiled out and had caught fire, but it hadn't exploded. It had just quietly caught fire and it was burning and there was a flame a yard high. I went over and turned it out. It was fortunate that I wasn't in there when the vapors ignited because that wouldn't have been so good! I don't think that people in the First

Chemical Institute ever did know how that room happened to be so black that day!

Dr. O.: They must have thought somebody was smoking kymograph drums or something in their facilities! How could one really compare perhaps Gomberg, Levene and Fischer as chemists? Did they have any similarities?

Dr. V.: Well, their personalities were very different. Fischer was a man of terrific power. If he had gone into politics he would have been another Bismarck! He was a big man--he was about 60 when I worked with him--his handshake was like an electric shock then! He looked like a typical German professor; he had a beard. But he was a man of terrific force. I was told that in his earlier days he'd had a terrific temper when things went wrong. I never saw it but once. He started me on a problem and I had to make some crystalline material to start it out with and we had some difficulty until finally I saw a method in the literature for making it. I got a plateful of beautiful crystals. When he came in I started to show them to him, but he said, "Schon gemacht;" already made! He said that the two Englishmen that butted in on this problem had done just what we were intending to do. He "panthered" up and down for about five minutes and then went out!

Dr. O.: Was he the egotist that Warburg apparently was?

Dr. V.: Well, I wouldn't say he was an egotist. He was a great man; he knew it but he was informal. With regard to this incident, there was a Saturday morning colloquium at 11:00 where everybody that had a doctor's degree went. At the next one Fischer reviewed this paper that these two Englishmen had done and reviewed it very fairly, and he said that he and I had started on it but that they had had the same idea and he was sure that their solution of it was correct. His first reaction was to boil over! But he was a great human being. He more or less ridiculed the superformal type of German official; he was a real man.

Fischer was a warm individual. He had a nephew named Gerlach that was also working with him--and he put Gerlach at the same desk with me. (The desks were about eight feet long and there would be two men working at each.) Gerlach and I became very good friends. Gerlach had taken his doctor's degree at Erlangen University. Most of the men that worked with Fischer already had their doctor's degree. Some of them were foreigners, but this boy came from Bavaria and he felt as much a foreigner in Prussia as I was. He was homesick for Bavaria! I had just come to Berlin with my wife, who had been a student in the University of Michigan, and we became very good friends with Gerlach and went around together evenings a great deal. Fischer was terrifically strict with Gerlach. It was very difficult for Gerlach to do anything that was right! Weekends Fischer would take Gerlach to his villa out at Wannsee, a lake outside of Berlin, and treat him like a son, but rather than show him any favoritism in the laboratory he leaned over backwards and was hard on the poor boy! Whitsuntide springtime came and everybody had a few days vacation. They make much more of it there than we do here. The vacation started on a Saturday morning, but Gerlach was so homesick to get back to Bavaria that he wanted to get a train Friday afternoon. He was working with a big porcelain dish in which he was boiling some stuff with lead oxide in order to precipitate chloride. It was supposed to make lead oxichloride which eventually would precipitate all the chlorine. It takes boiling a long time because lead chloride is fairly soluble; it's the slowly formed oxichloride that is precipitated. And Fischer told him to precipitate the chloride with lead oxide instead of silver, I don't know why but he did. Gerlach would boil it and boil it and take a drop out in a pipette and test it with silver nitrate for chloride and there'd be a precipitate and he'd boil it, put in some water and boil it again. Well, he'd boiled it all the morning and there was still chloride in it and he wanted to get his train in the afternoon and he knew Fischer would be coming in as usual about 2 o'clock so he said, "I do want to make this train, won't you boil this dish for me and if the "geheimrat" comes in he'll see it boiling and he'll think that I'm somewhere in one of the other rooms and that I haven't run away!" So after lunch I started it boiling and when it boiled down a little bit I put a little water in and all the other men--a dozen of them working in this room--one after the other, they got onto what was going on. An Italian was behind me and he would come and pour a little water in and then smile and the German that was next to him would come over and pour a little water in and smile and walk away! And then others took their turn. Well, sure enough 2 o'clock in the afternoon in comes "geheimrat" and you could have heard a pin drop! He came straight to my desk--right next to Gerlach's--and he went to the dish and picked up a pipette and took out a drop and tested it and there was still chloride in it, and he laid it down and walked off without a word. And then everybody began to talk and you could hear the room bubble up. (Laughter) So Gerlach got away and he wasn't slaughtered!

Dr. O.: That was close! How about Dr. Gomberg, was he that forceful an individual?

Dr. V.: No, Gomberg was very gentle. Very gentle. Very lovely personality. He lived with his sister. They came over from Russia when they were both, I think, something like twelve years old or so. Gomberg never got over his Russian accent. He was an exquisite worker. He did all his work himself; he didn't have a technician and he didn't have many Ph.D. candidates to share his work. At that time there was only one other Ph.D. candidate working with him. Gomberg had a laboratory about six feet wide and twenty feet long, with a window at one end of it. And out on one side there was a big laboratory where the elementary organic chemistry was being done. On the other side of his laboratory was a room about twenty feet square where two or three research men could work. I did my doctor arbeit in this special room. One of his teaching assistants was there and we worked together.

I was engaged, the last year before I took my doctor's degree, to a girl who was a senior, also taking chemistry; a very charming girl. She was due to do her organic chemistry laboratory work out in the big laboratory. Gomberg and his assistant knew I was engaged to her. They debated whether they'd put her out with the crowd or put her in where I was working. If they put her out in the crowd I would be likely to lose time going out to visit her and if they put her in the room where I was working, that might be distracting! So, the assistant told me about it afterwards, Gomberg said, "We'll flip a coin and if it's heads she goes out with the crowd!" Well, it turned out heads and Gomberg said, "We flip again." (Laughter) So she worked in the same room with me that year and that was very pleasant.

One time I needed a two-liter bottle. The only one I could find was one that had been used for making anhydrous ether by putting metallic sodium in it. That's the way you make perfectly anhydrous ether; the sodium has terrific affinity for water and it will take any water out of the ether. Well, if you put metallic sodium into water it explodes like a firecracker! This bottle had been used for ether, and I knew it, but it had been standing with these pieces of sodium in the bottom for apparently years. The sodium had taken up water and carbonate in the air and these pieces were all crusted. So I thought that probably there was no sodium left, but I knew there might be some, so I turned the water on in the sink, dumped the pieces into it, and stepped back to see whether anything happened. Flashes went off like cannon firecrackers and when it stopped, Gomberg looked in through his door and he said, "Now Van Slyke, you know what metallic sodium and water makes." (Laughter) I worked right next to him. Anytime I had anything to talk about he was right there. Those were days when your professor was not at a distance.

Dr. O.: Yes, that's so true. I imagine there are some instances where it's still this way, but certainly not at some levels.

Dr. V.: There are so many graduate students now that they can't have that intimacy. In Fischer's place he had a certain number of places.

He would only take so many people; about a dozen. The only reason I got to work with him was Levene who had worked with him before and knew Fischer personally--Levene arranged it. I worked with Fischer for a semester. Berlin was a lovely town in those days.

Dr. O.: This would be 1911?

Dr. V.: Yes. That was before World War I. Germany was the scientific center of the world. It was a tragedy that the military people of Germany got her into that war. They were the only ones that wanted it.

Dr. O.: That would be the period that was the tail end of the great migration of physicians to Germany and Austria----

Dr. V.: Physicians, chemists, physicists. I think probably Germany had more great scientists in practically all lines than all the rest of the world. Practically every outstanding scientist in this country had had part of his training in Germany. Levene spent two years in Germany. He graduated at Petersburg Military Medical School. He then came over with his family from Russia and went into private practice. He got tuberculosis, went up to Saranac and was cured. He decided that he could not resume the life of a practicing physician, and decided to go into biochemistry. He went abroad and worked for two years. Part of it was with Fischer. He came back and was eventually picked up by Flexner to start the Rockefeller Institute.

When the Institute started, the senior men were, with the exception of Opie, were men who for one reason or another would not be likely to be called to professorships in American universities.

Dr. O.: Why is that?

Dr. V.: Because they were foreigners! There was Levene who was a Russian. He didn't know anybody in American medical schools; he had no political route, so to speak. And then there was Carrel, a Frenchman, and a surgeon--experimental surgery--who got the Nobel Prize for a technique he worked out for suturing blood vessels. Then there was Dr. Meltzer who was a German from Riga, which had been part of Russia. But the cultural part of Riga was German. It was one of the Baltic towns. He came over to this country and went into private practice and also continued to do some physiology in his own home.

Dr. O.: He was primarily a respiratory physiologist, was he not?

Dr. V.: No, it was general physiology. The thing he was known for was his discovery of (I think he discovered it), the fact that when a muscle contracts, its antagonist relaxes, and he worked it out in studying the process of swallowing. And in Germany his common name was "Schluck" Meltzer. "Schlucken" means to swallow. "Schluck" Meltzer, because of that. And then there was Noguchi, the Japanese, who nailed the syphilis spirochete as the cause of softening of the brain. Well, Flexner was keen enough to see the possibilities of these men, and they were the men that the Institute started with. Opie, who had come from Hopkins, was the one man that had background in American universities and would be likely to get a professorship and he only stayed at the Rockefeller two or three years, then took a professorship in St. Louis.

Dr. O.: Yes, Washington University.

Dr. V.: Yes. But that's the way the Institute started; it was sort of a menagerie.

Dr. O.: I gather Dr. Flexner was really quite a good judge of men, although he may have had some help from people like Welch and others.

Dr. V.: It was Flexner's keenness of judgment. The Institute was what he made it. He got his men and then he backed them up and he personally handled the Institute. For example, I was with Levene seven years, then the Institute built a hospital and Levene and Flexner apparently talked it over and decided that I should be moved over into the Hospital and develop a department of chemistry in the Hospital.

Dr. O.: With the express idea being that though you would still be able to continue, to use a hackneyed phrase, in "basic chemistry" you would develop a department related to clinical chemistry.

Dr. V.: Yes. It was hoped I would take an interest in that. I was so distrustful of my ability to do that and so reluctant at leaving Levene, that I made Flexner write me a letter saying that if I didn't like it in the Hospital I could go back to Levene!

But I found that the young doctors in the Hospital were all just about my age and they took me in. I began to pick up medicine pretty fast; found it fascinating. So I stayed in the Hospital the rest of the time I was at the Rockefeller.

Dr. O.: One can really then put this decision, in a sense, in the lap of Simon Flexner. He's the one basically who decided that you were the man for this particular spot.

Dr. V.: Yes. In the Hospital, it was hard work, riding two horses, because I didn't give up my basic work. At the same time, I took up the study of kidney physiology and kidney diseases, but the young doctors that were there didn't know the field. I had to learn the story of nephritis and the physiology of the kidney and what goes with that from the ground up. And, although I was a chemist, I found myself in charge of a ward of patients with Bright's disease. Well, although I was very husky, apparently it took quite a good deal out of me and a clinician that came to work with us for a sabbatical year, that was Thomas Addis of San Francisco, he went over to Flexner and said, "Van Slyke is going to give out pretty soon unless you give him a year off."

Dr. O.: Addis of the Addis Count?

Dr. V.: Yes. Well, I didn't feel that way, but Flexner called me over. This illustrates the way Flexner handled things. He called me over to his office and he sat across the desk--he had piercing blue eyes--and he looked at me full, as though he was looking right through me, and he said, "Van Slyke, get your things in order and get out of here and go to Europe with your family for a year!"

Dr. O.: Gosh, just like that!

Dr. V.: Yes. He said, "I'm not inviting you to do this, this is an order!" If you had a thing that required a decision, you'd get it from

Flexner in about that time and it would be as good a decision as could have been made if he had spent months on it.

Dr. O.: What year would this have been that you took this trip?

Dr. V.: That was '29. So the family and I went to Europe and we spent the winter in Grenoble, in France. My children, who were in their teens, went to Grenoble University, or the high school, and picked up French and I, in a leisurely way, wrote one of the main chapters of Peters' and Van Slyke's Quantitative Clinical Chemistry, wrote the chapter on the acid-base balance.

Dr. O.: So you did stay out of the laboratory for that year.

Dr. V.: Yes. There was no laboratory to work in and no assistants to be responsible for.

Dr. O.: I'm trying to think, I should know this, but I just can't remember when Peters and Van Slyke, Quantitative Clinical Chemistry was published.

Dr. V.: It came out about 1930. I think the Interpretations came out in '30 and the Methods in '31. At least we spent ten years on that.

Dr. V.: The publishers came to Peters--Peters worked with me for a year just before the war and then he went into the Army and when he came out he went to Yale, but we kept in contact. The publishers came to Peters and asked him to write a brief manual on clinical chemistry, and he asked me to look over his chapters when he got them done. He sent me the first chapter and I went over it and made changes in it and then he said, "I can see that we have to do this together; it takes a chemist as well as an internist!" We thought we'd do it in one vacation, but it just grew and we didn't realize how much material there was and it was just about ten years before we got it finished. Some chapters took a whole year!

Dr. O.: It's still the classic and extremely difficult to come by.

Dr. V.: Oh, I think it was useful.

Dr. O.: Oh, I think there's no question that it, in a sense, revolutionized the whole field as far as the application of analytical chemistry to, again in quotes "clinical medicine." This was one of the things I'd like very much to dwell upon for a bit, if we might. Perhaps I might just turn this over. We're not at the end, but we're getting close to it and we won't be interrupted.

[End of Side I, Reel 1]

[Side II, Reel 1] Recorded May 27, 1969.

Dr. O.: I'm really not sure how to phrase the question, but when you entered the field of clinical biochemistry, I call it, perhaps unwisely, I'm not sure how you really refer to this branch, if you will, of biochemistry.

Dr. V.: Well, that's as good a name as any, I guess.

Dr. O.: Right. It really was--if in its infancy at all--just barely in its infancy. The work of yourself and your group at the Rockefeller Institute it seems to me changed the entire method, in many ways, of practicing medicine. It was originally a qualitative science and through the efforts of your group in this tremendously vast area an understanding of pH and its clinical implications and acid-base balance, electrolytes, and so on was developed. One ends up in going from the qualitative to really a quantitative type of medicine. I would imagine, at the onset of your career at the Rockefeller Institute, what one found as routine laboratory studies performed on patients were a totally different "kettle of fish" than what they were some 15, 20 years later. And really, your group is very much responsible for a great deal of this.

Dr. V.: We were responsible for part of it. There were others, of course, particularly Folin at Harvard and Benedict at Cornell Medical School. I think our group at the Rockefeller were closer to the clinical application; we were working in a hospital. Benedict was working in a medical school but not in a hospital. And it was the same with most of the other biochemists at that time. Most of the biochemists then were trained in a time when there was not a great deal of quantitative work done. You worked with proteins and peptones, and so forth. Particularly blood chemistry had just started to develop. We got into it because at the time I moved into the Hospital with my assistant, Glenn Cullen, the Hospital was starting to study diabetes. That was before the days of insulin, and the man who brought diabetes, so to speak, to the Rockefeller Hospital was F. M. Allen who had been working on it with dogs.

He made dogs diabetic by cutting out three-quarters of the pancreas. Up to that time the theory of handling diabetics was to get them to eat as much fat as you could. They couldn't burn sugar so you fed them cream and tried to keep their strength up by giving them the calories in fat. Allen fed some of his diabetic dogs a good abundant calorie diet mostly made up of fats, and others he put on semi-starvation. They were not completely starved but they were thin, and kept that way. Well, the dogs that were well-fed on calories were fine for a few months, but then their diabetes got worse and they died while the thin ones lived--their diabetes didn't progress. And Allen came to the Institute to try out what came to be called "the starvation treatment" for diabetes. His principle was to put the patient on a practically starvation diet. He fed them thrice-cooked vegetables; they were boiled three times so there was nothing left but bulk, to satisfy the desire for something in the stomach. And in a few days they would stop excreting sugar and the blood sugar would come down and then he'd start building up the diet to see how much they could tolerate. That was the only way that a severe diabetic could be kept alive until insulin came along. Well, the danger was that on this almost no calorie diet, acidosis could develop very quickly. Allen didn't think it could; the dogs don't have it. And he figured that if you didn't give them the fat which makes the ketone bodies, they couldn't make oxybutyric acid and they couldn't get acidosis. Well, one of the first patients we had who was put on this treatment was a middle-aged nice lady that came in, a typical middle-age diabetic, not terribly severe. She went into coma and died in a week!

Dr. O.: On this starvation diet?

Dr. V.: Yes. Something had to be done to see acidosis coming before it got too bad because once you go into coma you're finished. And so Cullen and I read up all the literature there was on acidosis and decided that the best clinical metnod would be to measure the plasma bicarbonate and the most practical way to do that at the bedside was gasometrically, and for that reason we developed the old handshaken CO_2 machine. Then later we got to doing more refined work on the physical chemistry of the electrolytes in the blood and we needed a more accurate procedure so we developed the manometric machine. With the old handshaken machine you measured the volume of gas at barometric pressure. You can measure the barometric pressure to a tenth of a millimeter which is about one part in some eight thousand, but in your volume you might have one or two percent error, particularly if you had a small volume. To make the accuracy greater, the stunt was to decrease the pressure and increase the volume until the volume error was brought down to somewhere near the pressure error was. That was the basis of the manometric apparatus. After we worked out the CO_2 method we didn't have any more deaths in coma because one could detect it by the analyses well before there were any clinical signs. The bicarbonate can go down to half normal and the patient isn't uncomfortable. He may be a little dopey, a little sleepy. He's breathing more deeply than normally, but you wouldn't see it unless you were used to looking for it because he doesn't breathe faster, he just breathes a little deeper. And then when he gets much below that, then, in those days, the coma would develop explosively.

Dr. O.: You also were deeply involved in studies in renal physiology.

Dr. V.: Well, the way we switched to that was that after some years Allen left and started a diabetic research institute of his own. He had brought the diabetic problem to the Hospital and the Director of the Hospital thought that it was fair to let him take it with him and not to compete with him. By that time I had become interested in clinical medicine and decided to take on another problem. I decided to take on the renal problem because there was a chance for quantitative chemistry there--measurement of function and the metabolic things that the kidney did. So we deliberately took on the kidney problem.

Dr. O.: Through those years certainly a considerable number of clinicians spent time working in your laboratory, many of whom went on in to be very much biochemically-oriented internists, if you will, professors in various departments.

Dr. V.: Yes, Hastings counted them up once and he said there were 70! One of them became Professor of Medicine in Oslo in Norway; two of them became Professors of Medicine in Copenhagen.

Dr. O.: Did Kai Linderstrøm-Lang work in your lab?

Dr. V.: No, no, I never worked with Linderstrøm-Lang and he never worked with me. The Danes that did work with me, the first one was Lundsgaard. He was the first man that did a blood pH with a hydrogen electrode, and he showed up one morning without any warning--a big,jolly fellow. He had already done so much that he had an international reputation, I knew his name. I came in one morning and everybody in the laboratory--I was a little late--was down in my office having a very good time and not doing any work. I went down and here was this big chap leaning back against the bench entertaining the crowd, and he looked at me and he said, "Uh, you Van Slyke?" I said, "Yes." He said, "Well, I'm Lundsgaard, I've come to work with you for a year!" He had decided he would do that and went down to the Danish shipping company and said that he wanted them to give him a job as ship's surgeon to get over to New York. He was the kind of fellow that got anything he asked for! Well, we worked together seven years, and then he went back and became Professor of Medicine in the University of Copenhagen. He was so interested in the techniques that we had worked out that he arranged to have Cullen, who was my assistant, go over there and work there in his clinic for a year to introduce methods. Then later Salvesen, who was with me several years became Professor of Medicine in Oslo. He's the king's physician at present! And then there was Eggert Møller who did a lot of the kidney work. He's just retired from the Professorship of Medicine at Copenhagen.

Dr. O.: Well, I know it's quite an army--a legion of people. How was your laboratory basically organized when you'd have people like Dr. Hastings there or Dr. Cullen? Was there sort of a common problem that the entire laboratory staff was working on or did each man have his own part of a common problem? Were you there as the "geheimrat"? Was it like Fischer's laboratory where these people were working on a project primarily of interest to Fischer?

Dr. V.: Yes, each man there worked on a problem. They all radiated from Fischer, so to speak. If a man came to work with me, he usually wanted to work in the field that we were working with--in nephritis, for example, after we got into that. And I would start him on a problem in connection with that. If he got an idea by himself, why, that was ok, he could work on it by himself. Or if two of them would get an idea together and wanted to team up, why that was ok. Or sometimes they would team up with people over in what was called the "laboratory part" of the Institute that was separate from the Hospital. There wasn't any rule, and you might say there was no organization! We just did work the best way that seemed desirable under the conditions.

Dr. O.: I know Dr. Hastings and I spent a fair amount of time talking about the work in hemoglobin studies and so on; Dr. Hastings was there and Dr. Heidelberger was involved in making hemoglobin for your studies.

Dr. V.: Yes, the blood gas work all developed out of the diabetes. That is, that got us started. That was the cause of developing the old volumetric CO_2 pipette. Then Lundsgaard came over and he was an internist interested in circulatory diseases, and he wanted to study blood oxygen in cardiac decompensation--you're an M.D. aren't you?

Dr. O.: Yes sir. Ex-surgeon, ex-pathologist!

Dr. V.: He wanted to see whether in decompensation the oxygen content of the blood decreases. That could happen either from pulmonary conditions where you don't get good oxygenation or it could happen from retarded circulation. Lundsgaard started doing blood oxygens--or he called it "unsaturations." He'd take venous blood and divide it into two and part of it he'd saturate with air and the other part he analyzed as it came. He at first used the Haldane apparatus for determining the blood oxygen. You have blood in a bottle that's connected with a little manometer and put ferricyanide in. As the oxygen comes out of solution the manometer goes up. From that you judge how much oxygen there is in the blood. It takes fifteen minutes or so before it comes to the top. Well, Lundsgaard kept on shaking the bottle after that, and he found that the pressure would start to decrease. It was obvious that some of the oxygen was being used up, and so he was very distrustful of the method. It turns out, later when Stadie tried it out--tested it out--in comparison with the manometric method that, the Haldane method was about ten percent low because there were some reducing substances, probably lipids, that used his oxygen up in the alkaline solution that was used. And that is why after it reached a peak it would start coming down, but if you took it up to the peak, and stopped then you had about 90 percent of the true value. But Lundsgaard didn't like it, and I said, "Well, I'm sure you can do it with this CO_2 pipette and get the answer quick before there is time for this consumption of oxygen to amount to anything." I was very busy at the time, but I said, "I'll find time to work it out pretty soon." Every morning after that he'd come to my door and say, "Van, have you got that oxygen method yet?" (Laughter) So I really had to quit everything else I was doing and work out the oxygen method. Then he was very happy. It worked. But that's the way we got started on oxygen. The various fields that went ahead in my laboratory started some on the original impetus from one man, some from another.

Dr. O.: All based generally on a clinical problem that he brings to the lab.

Dr. V.: Yes, or they might go into what you might call basic problems from the clinical problem. Lundsgaard was a great chap. After he'd been there a little while, he went out for an evening with some of the other young doctors and he saw a handsome woman on the floor of the hotel where they were having cocktails, dancing, and he thought he'd like to dance with her and he just went out and tipped her partner on the shoulder and danced off with her! (Laughter)

I got to discussing with him some problem--I've forgotten what it was--but we had somewhat different views on it, and it happened that at three o'clock in the afternoon I had an appointment to see Flexner about something. I said, "Well Chren, we'll have to finish this up later, I've got to go over and see Flexner." He said, "No, we're going to finish it up now. You take the telephone and you tell Flexner you'll see him later!" And so I did that!

Dr. O.: I gather from speaking with Dr. Hastings that within the Rockefeller Hospital there was really a very much open-door policy with exchange of ideas and so on amongst the various labs, but that this wasn't always the case in the Rockefeller Institute proper.

Dr. V.: Well, the Institute was organized, for the most part, around senior men. They were called members instead of professors, and it was a bit on the organization of European universities where each professor is pretty much dictator in his own department. The Hospital was less that way. When it started, the Director, Dr. Cole--I think he was 35--and everybody else was around 30. There were no senior older men like Dr. Meltzer was. Dr. Meltzer was a German and naturally things would go in his department as a German professor would organize things. Things were more, you might say, "free and easy" in the Hospital. You could work on practically anything you wanted to. If you wanted to start a new disease naturally you would settle that with Dr. Cole. But what you would do with it, what problems you take up with it, Cole would never attempt to dictate. When it came to appointments, if a man wanted to come to work with me I'd see Dr. Cole about it and if possible have him interview Dr. Cole, then Dr. Flexner would approve it and it would be approved by the Board of Scientific Directors. I never recommended a man that wasn't appointed. It was as informal as that.

Dr. O.: Could you give me your impressions of Dr. Cole? He certainly is an important figure in contemporary medicine.

Dr. V.: Yes. He was a very fine man, both personally and scientifically. I've heard it said that he was considered the brightest man that ever graduated from Hopkins at the time that he graduated. But he came to the Institute with the idea that the laboratory and the clinic would work as one organism. As the Hospital started out, most of the young men there that were working on patients did their own laboratory work. Eventually, laboratory procedures got so numerous and complicated that that was no longer practical, but that was the idea--Dr. Cole's idea--

that laboratory and clinic should not be separated. And they pretty much continued that way, that is, I always had a couple of chemists working with me that were Ph.D. chemists, but I also had usually four or five M.D.s working with me, but they also worked in the laboratory. All of them.

Dr. O.: You mean also in the clinic, while they were working-----

Dr. V.: Yes, they had patients, they were in charge of patients, but the idea was to have so few patients per doctor and that the doctor could also do laboratory work. And the idea was, furthermore, to have a few patients that should be studied as completely as possible rather than have a great many patients from whom you collected just what you might call routine data. And incidentally, that's the plan on which the Brookhaven Medical Department started and continues.

Dr. O.: How many beds do you have here?

Dr. V.: We have 48 beds, and all the patients--the same as they were in the Rockefeller--are patients who pay nothing and can, for that reason, stay as long as it is essential to study them. They are usually happy to stay. We deliberately started the Brookhaven Medical Department on Dr. Cole's principles. It would be fair to call it "The Cole Medical Department."

Dr. O.: In the early days of the Rockefeller Institute, what was the reaction amongst the academic community, in New York, in local medical centers, medical institutions, places like Columbia. I gather that there were people who worked in your department who were getting advanced degrees at Columbia while they worked at the Institute.

Dr. V.: Yes, I had three chemists who had bachelor's degrees when they came to work with me and it was arranged that they got a Ph.D. from Columbia while they continued their work in my department.

Dr. O.: I was just wondering whether or not there was any sort of "sour grapes" feeling toward the Institute from the surrounding academic community.

Dr. V.: I think there was very little of that and perhaps for the reason that we really didn't compete. We had so few patients. We've really hardly competed with t he other schools. Personally, I always had cordial relations with my colleagues in the other medical schools, in the medical schools in New York and elsewhere for that matter.

Dr. O.: I've seen it somewhere, I can't remember where, but somewhere the statement that the "university concept" of the Rockefeller Institute started when Detlev Bronk was the Director. This really seems to be an injustice because obviously, taking your department as an example, you were doing one devil of a lot of teaching long before.

Dr. V.: The Rockefeller Institute, before it became a university, was really a postdoctoral university. Most of the people that worked there up to that time already had their doctor's degrees. Not always. As I say, there were three men that started as technicians with bachelor's degrees and used their work at the Rockefeller as theses. But for the most part, the young men that came to work there were the same as I was, they already had their M.D.s or their Ph.D.s, and they would work there usually not less than two years--two to five, seven--and then go out to faculty positions in universities or to research or heads of research laboratories. It was, I think, definitely an educational institution. Bronk changed it to a graduate school that specialized on predoctoral students.

Dr. O.: Now really the change in name, I don't think, has changed the concept of what they've been doing for some while. It's just that they elected to take the name University as opposed to Institute.

Dr. V.: Well, the character of the Institute has changed in that the medical side of it is much less emphasized than it was. I think that was Bronk's idea. I regretted it. I think the school's a fine thing as it is now, but I was sorry to see the medical side of it gradually de-emphasized. Senior medical men have left and I don't think they've appointed others in medicine. And the Hospital was a definite sub-unit of the Institute with a very high morale under Dr. Cole and under Rivers after Cole retired, with a director as Cole and Rivers were. Now there is no hospital director, there's a Chief Physician. But the special character of the Hospital is not changed.

Dr. O.: Yes, it certainly sounds like a fair amount of deemphasis of medicine.

Dr. V.: Yes, and the Institute has a Professor of Philosophy, Professor of Mathematics.

Dr. O.: Have you seen this oral history memoir of Dr. Rivers that was done by Saul Benison?

Dr. V.: No, I haven't.

Dr. O.: It's quite interesting reading.

Dr. V.: I haven't. I must get it. Do you know who published it?

Dr. O.: Yes, M.I.T. Press. It came out in late '67 I believe.

Dr. V.: The author was Saul Benison?

Dr. O.: Yes, B-e-n-i-s-o-n. I know Saul quite well. He's been very interested in the Rockefeller Institute.

Dr. V.: That's the life of Rivers?

Dr. O.: Yes. It's called Tom Rivers: Reflections on Life in Science and Medicine, an Oral History Memoir. It's very interesting to hear the reaction of those who knew Dr. Rivers who have read it.

Dr. V.: The M.I.T. Press. Yes, I've heard about that and I must get it.

Dr. O.: I think some feel that there's certainly much of Tom Rivers there because it, again, is an oral history memoir which has been edited rather extensively, but for those like myself who only knew the man by reputation and by secondhand information, it seems to capture a lot of the flavor of what he must have been like. But many who apparently knew him felt that perhaps he should have been interviewed a few years sooner than he was. That it wasn't the Tom Rivers they remembered. He was a little embittered here and there. But it's quite a document really. It's an excellent panorama of this period at the Rockefeller.

Dr. V.: I never talked with him about it but I can imagine that he regretted the fact that he had no successor as Director of the Hospital. The Hospital is still running. We still have patients. But it wasn't long after Bronk came before he changed the title of the Rockefeller Institute for Medical Research, he dropped off the "Medical Research."

Dr. O.: Oh, I had forgotten that. Very interesting.

Dr. V.: And then after that it became the Rockefeller University.

At the time, I felt that we had enough universities, but there was only one Rockefeller Institute acting as a postdoctoral university. I would have preferred to keep it that way. As a matter of fact, the National Institutes of Health was modeled on the Rockefeller. So the world no longer, you might say, needed this as an example--that is, the old Rockefeller. As a matter of fact, when they were planning the National Institutes of Health, they came up and examined the Institute in order to use the physical plan on which the Institute was working.

Dr. O.: Plus, I'm sure, the close relationship with the Hospital to the Institute and the Hospital, in a sense, to the personnel having patient responsibilities as well as laboratory.

Dr. V.: The National Institutes of Health is a darn good institution though.

Dr. O.: Yes. I spent four years there, no I beg your pardon, six years--two years in the Surgical Branch of the Cancer Institute, and then after two years away, I came back and went through the Pathology program there. Two years at Path Anatomy and two years at Clinical Pathology.

Dr. V.: There are a lot of very fine men there. Anfinsen went back to Harvard and only stayed there a year and returned to the National Institutes.

Dr. O.: I didn't realize that. I didn't realize he's been off for a year.

Dr. V.: Yes. He took a Chair at Harvard, but he only stayed there a year. I never asked him why he went back. He's a great chap.

[Break for lunch]

Dr. O.: If you could, for the sake of the record, tell me about your experiences at the Peking Union Medical College.

Dr. V.: Yes. I was appointed Visiting Professor to go out there in the fall of 1922. That was the time when Hastings and I had gotten started on our studies of gas and electrolyte equilibria in the blood. We had determined at that time that the hemoglobin of the cells bound more base--or balanced more cation, whichever way you want to put it--than there had been any idea of before. In blood with a rather high pH, for example 7.6, about 50 percent of the cation in the cells was balanced by hemoglobin acting as anion. Well, it had been known for a long time that the concentrations of chloride and bicarbonate in the cells are much less than they are in the serum, and we had a hunch that the hemoglobin, acting as an electrolyte anion, was responsible for it. On the way to China, I had a couple of weeks on the boat to figure on it and got the idea that we had a Donnan equilibrium which you get when you have two solutions separated by a membrane and part of the electrolyte in one of the solutions is nondiffusible. So I planned a set of experiments to do with determinations of chloride and CO_2, total base, and pH in cells and serum to test this out. Well, at Peking, at that time, the Professor of Medicine was McLean who had been with us and with L. J. Henderson when we got started on these problems. The Professor of Chemistry there was Hsien Wu, of the Folin-Wu methods. As soon as I got to Peking, I laid this plan out before Wu and McLean. McLean had a riding pony that was very handy to get plenty of blood from. So we started the next day to put his blood under different CO_2 tensions and see how the theory worked out. There were a lot of analyses to do with each experiment. We ran high and low and medium CO_2 tensions and observed the effects on the shift of chloride back and forth and also the shifts of water in and out of the cells. One of the things we found out immediately was that in order to get meaningful concentration results, they had to be expressed in terms of amount of chloride or bicarbonate or whatever it was per kilo of water and not per unit volume--not per liter. Because in the cells, the hemoglobin takes up such a large volume, that is, the cells have only something like 80 percent of water. In weight, the cells have got about 34 percent of hemoglobin and something over 60 percent of water, and the hemoglobin, of course, takes up a good deal of volume. But as soon as we put our results on a basis of amount of chloride, bicarbonate and so forth per kilo of water, then the crystallizing meant something. I think that when that system of expressing concentrations was introduced was when we wrote that paper.

Well, I was there four months and we ran three big experiments. Wu really handled it. He had three Chinese technicians, and they got the glassware and everything ready for every experiment. Wu really organized the work. He did it so beautifully that we didn't lose a single experiment. Usually you work for about half a year before you find conditions that go, but we didn't lose anything. And that work resulted in No. 5 in the equilibria series. [Going to the bookshelf] I have a copy of it bound. There's one of the diagrams--that's the apparatus that we developed just for the determination.

Dr. O.: This certainly is one of the classical papers in the field of electrolyte and water balance.

Dr. V.: I think so. Additional factors have been added to the picture, but this work developed its main factors. The clear areas here represent osmotically active concentrations, and the shaded area represents hemoglobin acting as an anion, which is not osmotically active. Well, the clear areas osmolar concentrations in cells equal the clear areas for serum. So, inasmuch as hemoglobin anion is practically inactive, osmotically, there has to be a good deal more cation (potassium, mostly), consequently less chloride and less bicarbonate in cells than in plasma. Which explains why there's only about 60 percent the concentration of bicarbonate and chloride in the red cells that there is in plasma. This imaginary experiment starts with a low CO_2 and pH of 8. Then we run in CO_2 until the pH goes down to about 6.7 where hemoglobin is at its isoelectric point and doesn't bind anything, that is, it acts as a nonelectrolyte. So, this area here--if this is all osmotically active, you have a great deal higher osmotic concentration than you have here. And also, the ratio of the chloride to bicarbonate in cells is much lower than in plasma----the hemoglobin anion in the cells has been replaced by bicarbonate. The ratio of bicarbonate in cells to bicarbonate in serum is much greater than the chloride. Now, according to the Donnan equilibrium those anions must have the same ratio. So, chloride shifts to the cells and bicarbonate shifts from the cells out to the plasma until you get the ratios equalized. The process explains why, if you run CO_2 into the blood, the bicarbonate in the plasma increases. After these events you have a greater osmolar concentration in the cells than in plasma than you have here so that in the last diagram you have water passing from the plasma into the cells, and the cells swell until you get equal osmotic concentrations. That expains why the cells swell up when you run CO_2 in the blood. Well, that's a "nutshell" of what we worked out in Peking.

Dr. O.: I know Dr. Hastings has referred to this particular bit of work because he was so struck by the fact that you had sent this letter which essentially had the question answered; it was just a matter of filling in the values, as it were, when you started working in the laboratory. He still has that letter, by the way, which you probably realize!

Dr. V.: Yes, I know. He read it at a seminar we had in Ann Arbor a few years ago. No, it was a celebration they had here on my 80th birthday and Hastings spoke of it. He read a part of that letter. I didn't know he still had it!

Dr. O.: Oh yes. In fact there is quite a file of Van Slyke correspondence there.

Dr. V.: Well, we worked that out and I had a very good time in Peking, too. I took a Chinese lesson every day after lunch and then my wife arranged a little tour around some of the parts of Peking. Aside from that, there was nothing to do except these experiments, none of the things that waste your time when you're at home. So we finished that work in three or four months. There were a lot of details to work out; things to do more accurately------

Dr. O.: Yes, when you returned to the Rockefeller.

Dr. V.: -----when we got back.

Dr. O.: You were only at PUMC on one occasion?

Dr. V.: I was only there once, yes. I made friends that I still have, and involvements with Chinese friends which I still have and which got me into a lot of work during the war because when the Japanese attacked China in 1937, three Chinese--two of whom were physicians in New York--organized the American Bureau for Medical Aid to China to help the Chinese out and they got me to join them. I couldn't refuse because I was so sympathetic with the Chinese when they were attacked by Japan.

Within a rather short time, they made me President of ABMAC. I had that job for seven years and it took probably a quarter of my time. During the war, the American Bureau for Medical Aid to China was the organization through which the United Services for China sent medical help. The United Services was an organization that sent all kinds of help to the Chinese, and the American Bureau for Medical Aid to China was given the responsibility for handling all of it that went as medical help, which was about 2 1/2 million a year. And we were in cable contact with the Chinese doctors that were at the head of the Chinese Army Medical Service and also the Chinese Civilian Medical Service and I think did a pretty good job of giving them the things that they most needed.

Dr. O.: Actually, this was medical supplies and so on that were flown in, I assume, over the Hump.

Dr. V.: Yes, and we got other men to join the American Bureau, medical men that had lived in China and they knew personally the Chinese leaders. So that we didn't send them things they didn't want. One time there was a cholera outbreak in one area and they needed cholera vaccine quickly. We cabled all over the Pacific and within 24 hours they were beginning to get it!

Dr. O.: My Lord, that's amazing!

Dr. V.: It's the sort of thing you can't very well do if you're part of the government.

Dr. O.: That's right exactly.

[End of Side II, Reel 1]

[Side I, Reel 2] May 27, 1969.

Dr. O.: Certainly one of the names that to anyone who has been exposed to biochemistry and clinical biochemistry in particular, medical students and otherwise, is Lawrence J. Henderson, who is a very, I gather, close friend of yours. I wonder if you wouldn't mind saying a few words about him. I might say, obviously, as well as following along your career, it's always nice to get some flesh onto some of these names which to so many of us, who are not deeply in this field, they are names we see from the minute you start and yet you don't really have a picture of these people. I think it's very interesting and important that we have some sort of a record of what they're like.

Dr. V.: Yes. Henderson was a unique character. He was not much of a laboratory worker himself, but he was a great thinker, a generalizer. There is occasionally a scientist who comes along who is tremendously valuable in pulling things together that have been uncovered by other men and is stimulating. Usually, I think the generalizer who doesn't work himself is not likely to be one whose generalizations are worth a great deal because he doesn't have the sense of -----

Dr. O.: Perspective, possibly?

Dr. V.: -----perspective of relative values, of probable explanations against the improbable ones. But Henderson did have that sense. He did do some work himself in his early days. I first came in contact with his work when Cullen and I ran up against the problem of acidosis in diabetes. We read up literature that might be helpful, and the paper that really got us steered on our work was a paper by Henderson on the acid-base balance of the blood, that was published in German, in which he brought out the Henderson equation and pointed the importance of bicarbonate as the alkali reserve of the blood. Then I got personally acquainted with Henderson; I had met him before that but I got better acquainted with him. McLean had worked with Henderson for awhile. McLean, when Henderson was working on this problem of what it is that makes the difference between cell and serum electrolytes; Henderson collected the data but he didn't have the explanation that we got when we found that hemoglobin bound so much alkali. He didn't know what it was that caused the difference, but he collected the data and he published a complicated nomogram that showed how much chloride shifts if you have a shift in bicarbonate or vice versa, and how much an oxygen shift causes a shift in the other things, and so forth. It was the discovery of the amounts of alkali that are bound by reduced hemoglobin and oxidized hemoglobin that Hastings and I worked out that gave the key to why these differences are. But Henderson laid out the problem in showing that the differences were there and approximately what they were. There was not accurate data available until we took the problem up and developed methods particularly to get the data. But Henderson saw that the problem was there and outlined it clearly. He was really a great man. Instead of being miffed because we got the final solution, he was delighted! There were quite a number of men that worked with him, all of whom developed into leaders. There was W. W. Palmer, who became Professor of Medicine at Columbia. Palmer came and worked with me for a year or two after he left Henderson, then he became Professor

Medicine at Columbia; and Redfield who stayed in physiology at Harvard; Binger, who came and worked at the Rockefeller, eventually went into psychology.

Dr. O.: Oh yes, I remember Dr. Hastings mentioned he was the well-dressed chap.

Dr. V.: Yes, he was always in good shape. Anytime you were with Henderson you felt rewarded. He had a camp up in north Vermont near the Canadian border and one time there were five of us went up there and spent several days with him just talking aside--Palmer and Binger, and Arlie Bock, who did quite a good deal of the work. Some of the work that we did on horse blood was repeated in Henderson's laboratory on human blood, and Arlie Bock and D. B. Dill did a good deal of the work. Dill was the man who led the expedition to the Andes that Hastings was due to go on, when Hastings was diverted to become a Professor at Harvard.

Dr. O.: Yes, that's where the name is familiar.

Dr. V.: Henderson had bought this small farm up in north Vermont and built a very delightful cabin on it, or villa, whichever you would call it. It was beautifully arranged. He loaned it to me for two summers when he was in Europe, so I went there with my family. There was a barn on it and he got the idea of fitting the barn up for a laboratory, so that his men could come up there and work in the summertime. He figured it would cost five thousand dollars. I went to John D. Rockefeller, Jr. and asked him if the Rockefeller Foundation could provide the five thousand dollars, and he said, "No, Professor Henderson has got other friends that can do that!" He said if he was stuck for five million, he said, "We'd begin to think about it!"

Dr. O.: Oh my! I guess it was such a small request.

Dr. V.: I can understand the Rockefeller Foundation doubtless got hundreds of small requests coming in and it would just have been administratively impossible to look them all up and decide whether they were worthwhile or not. So I think what they did mostly was to decide themselves what they would support rather than wait for other people to request it.

Dr. O.: Certainly another name which goes along with the textbook, Peters and Van Slyke, I understand Dr. Peters--Jack Peters, as he was known--was a rather interesting individual.

Dr. V.: He was.

Dr. O.: One who stood his ground when he thought he was in the right.

Dr. V.: He was a great fellow. His technique in the laboratory was beautiful. He had extraordinarily good hands. He was very good at drawing. When he was in medical school, McCallum was writing his textbook in pathology and Peters drew some of the figures in that.

Dr. O.: Oh, for heaven's sake, I hadn't realized that.

Dr. V.: Peters told me that. In the Peters and Van Slyke quite a number of the drawings in the _Methods_ volume, Peters made them. He was precise and exact and it was the same way in the laboratory. He was red-headed and loved an argument! When we started writing the book together after he asked me to join him on it, the first chapter he sent me I made quite a lot of additions and changes in it and wrote him a letter, as I remember, explaining why I thought there should be some changes and got back a letter arguing why they shouldn't be made. Eventually, we got it straightened out, but after that I merely revised every chapter he wrote--sometimes he wrote the first draft and sometimes I would. I merely made my revisions and sent it back without comment and then it was all right! (Laughter) But if I started to justify them that brought an argument.

One time there was a meeting of a Federated Biology Society in Montreal. I didn't go to it, but Peters and Cullen did and they stopped at my house in Bronxville, where I was living then, on their way home. They spent the night with me. Well, in the evening as we were sitting by the fire-side, Peters expressed some view about a physiological point--I've forgotten what it was--and Cullen said, "Yes, I think you're right," and added some reasons for it, and Peters said, "No, you don't agree with me and these things are different. You don't agree with what I said at all." Well, then an argument started. Peters trying to persuade Cullen that Cullen didn't agree with him and Cullen trying to persuade Peters that he did agree and it came 11 o'clock and my wife excused herself and went to bed. And it came 12 o'clock and I said, "Well, we'll finish this in the morning," and I put the fire out! (Laughter)

Dr. O.: He's quite famous for that.

Dr. V.: Yes, he loved an argument. But he was a beautiful worker and tireless!

Dr. O.: He wasn't Department Chief at Yale, I don't believe, I think Dr. Blake--Francis Blake--was Professor of Medicine when Dr. Peters was there.

Dr. V.: They were both Professors. I don't know what the organization was with regard to the chairmanship. Peters was in charge of metabolic diseases and Blake of infectious diseases.

Dr. O.: Well actually, Francis Blake had spent some time at the Rockefeller, had he not?

Dr. V.: Yes.

Dr. O.: Did you know him perchance?

Dr. V.: Oh yes.

Dr. O.: His son is my Chief.

Dr. V.: Is that so?

Dr. O.: Yes, John Blake, John B. Blake is the Chief of the History of Medicine Division at the National Library of Medicine.

Dr. V.: Oh, is that so, is that so, how interesting. Yes, Blake was there in the early days, worked on pneumonia. The first clinical problem attacked by the Rockefeller Hospital was pneumonia and it was very much involved in the epidemic of influenza and the pneumonia that went with it in the 1918 flu. In connection with that, I think one might say that the Rockefeller Hospital started modern oxygen therapy.

Dr. O.: That's very interesting.

Dr. V.: It started this way. Lundsgaard, the Dane that came to work with me was interested in blood oxygen and he was an inspiring type of individual; he got everybody interested in blood oxygen. One of the things he was interested in was cyanosis and he worked out the conclusion that you get cyanosis when there's five grams of reduced hemoglobin per hundred ml. of blood in the capillary blood, taking the capillary oxygen content as a mean between the venous and the arterial. You can't get cyanosis if you have severe anemia because you don't have enough hemoglobin there to make that five grams of reduced hemoglobin. Lundsgaard and I wrote a monograph on cyanosis and that conclusion was part of it. The influenza epidemic came and the severe patients that got the pneumonia that complicated the flu, the more severe ones were cyanotic, and it was a very grave time. And Stadie, who was working with me and also working on the pneumonia service and knew of this work that Lundsgaard was doing, was interested to see whether these cyanotic people were cyanotic because they couldn't get oxygen into the blood and the lungs or because they had a retarded circulation. So he started doing arterial punctures. That was the first time arterial punctures were done in what you might call a clinical sense. A German had worked out the technique on animals. When Lundsgaard and I proposed to Dr. Cole that we try it on ourselves, Cole said, "No, that's too risky to do it on human beings."

Well, Stadie got the idea, while Dr. Cole was away on an inspection of army camp hospitals, and he didn't know that it was forbidden, and I was home with the flu. When I got back, Stadie had already worked out the technique on dogs and done it on himself and on one or two patients, and I had him do it on me and it went all right. So, by the time Cole got back from the army camps, arterial puncture was a fait accompli! That's the way it got into modern medicine.

Well, Stadie very quickly found that when these patients got cyanotic there was a lack of oxygen in their arterial blood; they weren't getting oxygenation of the blood in the lungs. And he thought that it might be overcome by increasing the oxygen content of the air they breathed. So the way it happened, Stadie had had an education as mechanical engineer before he went into medicine. So he built an oxygen chamber that would hold two patients--hold two beds. It was air-conditioned--that was before air conditioning was known, but it was air-conditioned so that it didn't get hot, and he had a regular Goldberg arrangement to analyze the oxygen at intervals and automatically regulate the inflow so that the oxygen would be kept where you wanted it. Well, he found that--well to take a typical case, a patient with 70 percent oxygen saturation of his arterial blood instead of a normal 98 percent saturation, would have mental disturbance and tachycardia. When he was put into the chamber with 60 percent oxygen in the air his arterial saturation went up to over 90 percent his mind cleared and his heart slowed down.

Dr. O.: This was without any attempt to use a mask or nasal tubes, just the environment, the inner chambers.

Dr. V.: No, the idea was that in order to feed, bathe, etcetera with the least tiring of the patient, the best way was to have a chamber. It was all glass. You could see in from anywhere. It was put in a large ward chamber. In the air with 60 percent oxygen, the anoxia would be immediately relieved. If the patient was delirious he would come out of the delirium, his pulse rate would come down. The oxygen didn't affect the course of the infection, but it gave the patient a chance to fight it. He didn't have to fight severe anoxia together with the bacterial toxin. The patient's blood was analyzed for oxygen so that it was known what was happening. That work, I think, really started analytically controlled prolonged oxygen therapy in this country, as a matter of fact, in the world because it hadn't been used before in a systematic way. It had been used in a haphazard way by putting a mask over a patient's nose and mouth and bubbling oxygen out of a tank, but without any accurate knowledge of what concentration of oxygen was being given and without analyzing the blood for oxygen to find whether anoxemia existed, whether it was remedied by breathing oxygen-enriched air, and when the patient's pulmonary condition improved so much that he could be taken out of the chamber.

On Long Island there's a Catholic hospital, for circulatory diseases, between here and New York, where they have children with congenital cardiac trouble that have anoxia from left to right cardiac shunts, and they have a room there that's modeled on Stadie's that will hold five kids at once and they keep them in there for weeks. Well, you might say that was the result of this Dane, Lundsgaard, coming over and getting us interested in oxygen!

Dr. O.: It's amazing really how many things can come out of a purely happenstance occurrence. I mean, an individual literally knocking on your door saying here I am!

Dr. V.: Yes. Lundsgaard was a great chap. Lundsgaard persuaded me to work out for him the method for determining oxygen in the blood that was used soon afterwards by Stadie. We laid out the outline to the book on cyanosis by going down to Lakehurst, New Jersey for a week--Lundsgaard and I. We worked on the book every morning and played golf every afternoon. By the end of the week we had the book outlined!

Dr. O.: Yes, that's listed here, 1923.

Dr. V.: It was rather a monograph than a book although it was published in book form.

Dr. O.: While we're speaking of the book, I understand Volume 2 of Quantitative Clinical Chemistry has been republished, didn't Peters put out a second volume? It's a modification or shortening or something, but was there ever any talk of a complete revision?

Dr. V.: Yes. We promised the publishers we would keep up the revision of the whole thing. I got so involved in laboratory work, also this China medical work, that I just didn't do it, much to Peters' disgust. Eventually I told him to go ahead with the Interpretations. He agreed to that and he started. Then he said I'd have to do the last half of it with the acid-base balance and the hemoglobin and oxygen which was practically based on work which was mostly done in the Rockefeller Institute laboratory and I said I would, and he agreed to revise the first half. Well, he carried out his part and revised it and I never did carry out my part. But there was so much demand for the unrevised second part, which was to a considerable extent, a finished job, that the publishers have recently republished that, the last half, without revision except for correction of a few errors. I feel very much ashamed that I never did do my job on that but the war came along and the American Bureau for Medical Aid to China and then this job at Brookhaven organizing the medical department.

Dr. O.: You were busy, to say the least!

Dr. V.: So I just failed. And now the applications of clinical chemistry are so numerous that nobody could write one book to cover the field.

I am engaged at present on a book--a purely technical book--to bring together in one volume the various applications that have been made with the old manometric gas analysis machine. A lot of things have been done with it in various laboratories that I never anticipated it would be used for. It's used for extracting and measuring gasses for chromatography, for example. I've got a man from another laboratory who's developed those methods to write a big chapter on it.

Dr. O.: I'm sure it's difficult and perhaps almost unfair to ask you a question like this, but, and I don't mean to sound maudlin at all, but what of this vast amount of work that you and your group have done do you consider the most important, or do you think any one group of experiments, as you look back with the perspective of the succeeding years, was perhaps the contribution that's had the greatest impact?

Dr. V.: I presume the work that had the most impact, because it was taken up and applied, was the work on the acid-base balance. The series of papers that we published on the blood gasses and electrolytes, including that one from Peking on the physical chemistry of the blood, was more refined and went further, but it has not been understood to the same extent; that is, relatively few people would be able to tell you what that Peking paper was about. It goes into the thermodynamics of the Donnan equilibrium and the biochemists, at the time that that was published in the early 1920s, most of them weren't equipped to appreciate that sort of thing and probably never read it. But the acid-base work was needed. There was an application--you might say there was a vacuum that it filled. So that it probably had the most impact on internal medicine of anything. Of course, the work we did on renal physiology and Bright's disease have been taken up rather widely, too, and clinicians do urea clearances and other clearances all over the world.

Dr. O.: That's a routine hospital laboratory procedure now.

Dr. V.: At the time, while I was still in Levene's laboratory, I worked out the nitrous acid method for determining amino acids, and, with the help of Gustav Meyer, showed for the first time that free amino acids are absorbed during digestion and that there are enough absorbed to account for nitrogen metabolism. That had a marked impact on physiology at the time. I don't think it ever affected clinical medicine. There had been so much work done, and since chromatographic methods for micro-determinations of amino acids have come out--so much of that--that I think it's only an occasional historical review that would recall that work that Meyer and I did. That came out about 1912. It isn't very often that a piece of work is remembered for more than a decade.

Dr. O.: It's rather amazing. This is so true. You look at bibliographies of papers written today and one almost gets the impression that they don't want to have a reference which goes to, say earlier sometimes than 1964 or 63, so you know everything has to be built from the latest building blocks.

Dr. V.: I've been shocked to encounter two or three Ph.D. chemists that didn't know who Emil Fischer was! Modern ones. He was the world's greatest chemist in his day and he did enough to make five different men immortal. His work on the aniline dyes; he worked out the structure of the purines, the pyrimidines. He worked out the structures of the sugars on which all sugar work is based. He demonstrated the amino acid constitution of the proteins and in his later years, he worked on the chemistry of the tannic acid series of compounds.

Dr. O.: It's a rather sad commentary. It's true in medicine, too, that everybody's in such a hurry to learn new things and develop new things seemingly.

Dr. V.: There's just so much to learn. You could keep up with science fifty years ago when I started. For a number of years I abstracted the Biochemische Zeitschrift and Zeitschrift fur Physiologia et Chemie. Those two journals had almost all the biochemistry there was in them, and one man could abstract them for the American Chemical Society. Now I couldn't abstract the Journal of Biological Chemistry. Some of the papers involve elaborate techniques that I have never used and couldn't understand. That is, I'm not capable of covering everything that comes out in biochemistry, which I was able to do in the early years.

Dr. O.: Did you ever feel at any time that not having an M.D. was a hindrance as you were working more and more in the field of clinical biochemistry?

Dr. V.: Well, I don't think it was a real hindrance because I always had good M.D. men to collaborate with. I would have been glad to have an M.D. training, but it would have taken six years additional and during those six years I made an awful lot of progress in biochemistry. I had enough biology so that working with men that were trained in medicine, I could understand what they were doing. And, as a matter of fact, I became a pretty good clinician on Bright's disease! I made the rounds regularly.

Afterwards, in two or three papers that have come out under my name that were lectures, the M.D. was added without my knowing it! One of them was before the American College of Internal Medicine, in Chicago. I gave a lecture on shock kidney and was granted what you might call an honorary M.D. when it came out with my name on it. I did get honorary M.D.s from two foreign universities, Oslo and Amsterdam, which pleased me very much.

Dr. O.: Well, I certainly didn't mean to intimate in any way that you should have. I was just curious to see how you felt or would react to that question because God knows, it would have been "gilding the lily"---I mean, it wasn't something obviously necessary to have.

Dr. V.: I would have been glad to have it, but it would have cut out several years of very valuable experience in biochemistry.

Dr. O.: Alma Hiller was the associate in your laboratory for some years, was she not?

Dr. V.: Yes. She was with me 30 years. She came--I think it was about 1916 or 1918--and she stayed with me until I reached the retiring age in '48. She had a Bachelor's degree in chemistry and she took a Ph.D. at Columbia while she continued working with me. She really ran the clinical laboratory----after we developed what you could call a "Clinical lab" she really ran it.

Dr. O.: In other words, the service laboratory, as it were, for the Rockefeller Hospital, for the routine clinical lab work.

Dr. V.: Yes, and she also did research work. She was a good chemist.

Dr. O.: L. E. Farr. Is this the same Dr. Farr who came here to Brookhaven?

Dr. V.: Yes.

Dr. O.: He was with you in the thirties, wasn't he?

Dr. V.: Yes. He left to become head of the Alfred I. Du Pont Institute in Wilmington, and when I took over the job of organizing a medical department here, I got him to leave Wilmington and come out here as head of the Medical Department.

Dr. O.: I was just looking through your bibliography and I see this paper by Phillips, Van Slyke, et al which is another standard in the blood bank.

Dr. V.: The copper sulfate method?

Dr. O.: Yes. To test someone's hemoglobin when they came to give blood.

Dr. V.: Yes. This is how it happened. The war broke out and I was called to Washington on a committee to talk over things that were needed in the army medical hospitals for field service. It occurred to me that a specific gravity method for blood concentration would be useful. Dropping methods had long been known using mixtures of organic liquids such as benzene and chloroform. Chloroform being heavy and benzene light, one can make a series of mixtures of varying specific gravity. The mixture in which a drop of blood neither rises or falls has the same specific gravity as the blood. However, such organic mixtures were not practical for field service because they have temperature coefficients about five times as great as that of water or blood. They give accurate results only if used with a constant temperature bath. We needed to have gravity standards in the form of water solutions. But a drop of blood falling into a solution of sodium chloride, for example, disintegrates. My first idea was to use sodium chloride solutions containing picric acid, which would form a sack of protein precipitate around the blood so that it would not disintegrate. It worked all right. But the next morning Phillips with a copper sulfate solution, which was just one substance did the same thing. It also had the advantage of having a characteristic color, so that one would know what was in the bottle, and copper sulfate solutions turned out to have the same temperature coefficients exactly as the blood or plasma in which they balanced. So we developed the copper sulfate method for blood specific gravity. From the gravity of plasma one could estimate the concentration plasma proteins, and from the gravity of whole blood one could estimate the concentration of hemoglobin. So we developed the copper sulfate method. It was adopted by the armed services of both our country and Britain, and was used especially to assay the effects of shock and hemorrhage in wounded men. The way in which it came to be applied by the Red Cross to test blood donors is interesting. I was on the Blood Bank Committee, which decided that 12 grams of hemoglobin per 100 ml. below which blood would not be drawn from a donor. Reports came in from all over the United States concerning the percentage of volunteer donors that had the required concentration of hemoglobin. Some cities reported refusal of very few donors and others reported so many rejections that it looked as though they had an epidemic of anemia. It was apparent that the variations were probably due to errors in the various methods for hemoglobin determination. We adopted one copper sulfate standard that would balance blood that had 12 grams of hemoglobin per 100 ml. If a drop of blood fell to the bottom of the solution the hemoglobin was above 12 grams and the donor was acceptable. The standard solutions were sent from a central laboratory all over the country. All the geographical differences in hemoglobin disappeared. The test was just a matter of drawing a drop of blood from a finger or ear and letting it fall into the copper sulfate solution. If the drop sunk you were a donor. Phillips was a great fellow. He has been working for several years on cholera in the Orient.

Dr. O.: Yes. In the Naval Medical Research Unit in Taipei.

Dr. V.: Yes. I went out there in '61 and worked with him for a few months. He is both a beautiful laboratory worker himself and a great organizer of teamwork. The success of the method that he developed for treating cholera was extraordinary. In the old days, cholera was practically sure death if one was not treated, and 60 percent chance of death if one got the best hospital treatment. I remember reading an old health report from the Philippine Islands where the mortality from cholera was given as 99 percent. In hospitals where Phillips' treatment was applied there was almost zero mortality. Even patients that were brought in practically moribund, recovered. They were infused with the special physiological solution of salts, that Phillips had worked out to replace losses. The infusion was continued until the specific gravity of the blood, taken with the copper sulfate method, was lowered to normal, indicating that the desiccation had been corrected.

Dr. O.: This was by careful monitoring of their electrolytes, water-balance and so on.

Dr. V.: Yes. He had worked out the relative losses of potassium, sodium, magnesium, calcium, chloride and bicarbonate that they lost in their stools.

Dr. O.: I should have said that good replacement then.

Dr. V.: Yes, he'd worked out a routine of good replacement, a solution, you might say. And he'd give enough to bring the specific gravity of the blood down where it ought to be; the specific gravity would be very high because of desiccation. He put the patient on an army cot, which was nothing but a stretch of canvas, with a hole in it beneath the anus and a pail beneath that, and then run the solution in as fast as the patient ran it out in the pail. And they practically all recovered! His prize patient took 80 liters in four days! But you could die in a few hours from desiccation. You go into shock and you just die. Plain desiccation. The extraordinary thing was that none of Phillips' crew caught the cholera. He'd have about a dozen men that would go to Manila, for example, and set up a unit to handle these patients. You couldn't handle them under the conditions without a chance of getting feces on your hands. You couldn't handle them. But none of the crew got it and very few Europeans got it and Phillips' explanation was that if you were in a good state of nutrition you had resistance to that type of cholera that was going around. That doesn't apply to every kind of cholera.
In 1911, when I came back from Fischer's laboratory--I made a trip through Europe and came back from Naples, stopped at Rome on the way. The second day we were in Rome we were told that cholera had broken out the first day we were there, in a certain section of Rome, and that the next day

80 percent mortality! I thought I had it myself! After we got on the boat, everybody had to tell where he was for ten days and so forth and it was rather expected. Well, the second day out I woke up with diarrhea and that rice water stool and wondered whether I'd be alive in the morning when the ship's surgeon came around. He was this fellow I told you about. He just felt me and he said, "No, you haven't got cholera; you'd be cold. You're warm!" It turned out there were bad oysters that had been brought from New York and were being used on the way back. There were quite a lot of people who came down with it. But that was true. This desiccation brings on a state of shock and you shut down your----

Dr. O.: Peripheral vascular system.

Dr. V.: -----peripheral vascular system and you get cold.

Dr. O.: I understand John Plazin was your technologist for many, many years at the Institute and then came here with you to Brookhaven.

Dr. V.: Yes. He was already in the Hospital when I moved in. Canby Robinson, I think, had brought him in. I don't know how Canby came to pick him up because he had only a high school education and he knew a little chemistry, but he was a natural born technician. He could do fine mechanics. I taught him glassblowing. I was a pretty good glassblower by the time I took my degree at Ann Arbor. I taught him glassblowing and within a year he was so much better than I that I never did any more! Immensely dignified man. Read the best literature and enjoyed the best music. Essentially a gentleman and a scholar despite the fact that he never had a college education! He was with me all the time

I was at the Rockefeller and then he came with me out here and he was here until just as I got back from Taiwan at Christmas, '61. He finished a week's work and he didn't show up Monday morning and I went over to his house and he was dead on his couch with the paper beside him! His wife had died some years before so he was living by himself.

Dr. O.: There's one question I would like to ask which more or less comes to mind any time that one sees somebody who has spent as much time as you have at a single institution. You obviously, over the course of years, had many opportunities and approaches, I'm sure, to go to various universities. I guess the reason for not doing so was being quite satisfied with the laboratory situation you had at the Rockefeller.

Dr. V.: Yes, I had everything I wanted to work with and complete freedom to do what I wanted. The most difficult thing to refuse was an invitation to go back to my alma mater, Ann Arbor, as Dean of the Medical School and Professor of Biochemistry. As I said, my father was on the faculty there when I was born and I played in the streets of Ann Arbor when I was a child. I graduated there and my first wife graduated there, and sentimental attachments were very strong. I knew most of the men on the medical faculty at the time and they were very cordial in their invitation. I agonized over it for a couple of months and finally decided that I'd keep on with the work I had going. I was a little afraid of administrative work because a good administrator has to know how to say "no" and I hate to do that.

Dr. O.: Didn't you, as the head of your laboratory, though, have to occasionally say no, in a sense?

Dr. V.: Oh, practically not. There were just a bunch of us working together. If one of my men got an idea that I thought wasn't any good, I let him find it out for himself and sometimes he was right!

Dr. O.: You stayed on at the Rockefeller Institute until the compulsory age for retirement?

Dr. V.: They had a compulsory age for retirement at 65, but I could have stayed on as an emeritus with my laboratory but without patients, and I expected to do that but the challenge to come out here and get a new Rockefeller Institute started at Brookhaven was attractive and so I rose and took the bait.

[End of Side I, Reel 2]

[Side II, Reel 2]

Dr. O.: Would you describe Dr. Dochez?

Dr. V.: A delightful fellow. He was very attractive. He was a bachelor all his life and was most popular as a guest for weekends or any other occasion. He never seemed to read very much but he always knew the literature. He seemed to be able to lie down on a couch with a book on his chest and wake up and know everything that was in it!

Dr. O.: That's a talent!

Dr. V.: He had one of these absolutely clear minds. There was no confusion in any of his thoughts. He lived with Avery as long as Avery stayed in New York. They had an apartment for three men and various colleagues were with them for shorter or longer times and then they would get married, one after the other, but neither Avery nor Dochez ever married. I remember staying with them one night. Dochez seemed to feel rather guilty that he was somewhat active socially as well as scientifically. And this was a Friday night and Dochez had accepted an invitation for the weekend and it bothered his conscience a great deal that he should be wasting his time on things like that and besides that he was sure that he'd be bored and he thought he'd call up and tell them he wouldn't come anyway. This would be a wasted weekend. No way for a man to spend his time on things like that. At the same time, Dochez was packing his suitcase! After awhile Avery went to the telephone and called a taxi to take "Do"! (Laughter)

Dr. O.: I gather Avery was known as "the Fess".

Dr. V.: Avery was known as "Fess". He also had an extraordinarily clear mind. He was a natural born comedian, Fess was.

Dr. O.: One looking at his photograph, you wouldn't think that. He looks very studious. Very scholarly.

Dr. V.: I remember one time he imitated a chimpanzee that was being tried out by a psychologist to see how the chimpanzee would figure on how to get a banana in a cage where he had to reach with a stick under the cage door to get it. And it was a convulsion to see Avery take that chimpanzee off. He could make a comic strip out of most anything that had something amusing to it. Perfectly deadpan!

Dr. O.: Could you give your impressions of Dr. Jacques Loeb?

Dr. V.: Yes. Well in Loeb's time, you might say there were two schools of biological thought. One school thought that living organisms were organizations based on the laws of physics and chemistry and that if you knew all about them you would understand how they work. Loeb belonged to that school. It was almost a religion with him. The other school of thought was that of John Scott Haldane, the great English physiologist who did all the work on the blood gasses and altitude and diving and so forth. Magnificent man! Haldane thought that there was some kind of vital principle that living cells had that we didn't know about--that was not explainable. It was something like the difference between Niels Bohr and Einstein. Niels Bohr felt that in the organization of atoms there were things that you could find out and express mechanically, but you could never make a mental picture of how they work. You could know what was going on and write formulas that would express it, but exactly what made it all go on, Bohr thought we probably would never know that, while Einstein was more optimistic. Einstein thought that there was an ultimate truth and that if you knew it all, you could make a picture of it. I understand that at Princeton they had very friendly arguments about it. Well, Haldane felt that there was an essence of life, or whatever you call it, that is essential for living cells, and this can't be defined on the laws of physics and chemistry, while Loeb felt that if you knew enough about it that you could so define it. And Loeb's object in life--at least one of his objects in life--was to work out the physical and chemical explanations of what goes on in cells as far as you could, and contract the area of the unknown. The idea was that eventually you might eliminate it. But at any rate, if you can get physical and chemical explanations of various mechanisms in the cell, you have added weight to the hypothesis that eventually such things are explainable if you could find out enough, and perhaps make progress towards finding such an explanation.

Dr. O.: It's interesting. Along these lines, another figure of this period, Alexis Carrel, at least in his later years became very interested in almost a mystical philosophy.

Dr. V.: Yes, Carrel had a mystic streak in him. Sometimes, sitting with Carrel at lunch, he would talk about some of these peculiar things and seemed to have a twinkle in his eye. I never realized that he took it so seriously until his book Man the Unknown came out, then I realized that he did take it seriously; that this mystic thing was real to him.

Dr. O.: I can't remember the date of publication of that book. Was it after he left the Rockefeller and returned to France?

Dr. V.: I think he was still at the Rockefeller, but I'm not sure. He didn't go back to France to stay until the war came on and then he went back to take part in that. Oh, I may be wrong about that, but it was about that time.

Dr. O.: Was he somewhat of a recluse, or was he fairly outgoing?

Dr. V.: Well, it would be difficult to describe him either way. He belonged to the Century Club--had friends there. He had friends in the medical profession. He had a good many visitors from abroad. He remained completely French, although he spent the last 40 years of his life in this country, and he owned an island off the coast of Brittany. He used to go back there every summer. He did his work mornings. He'd come at 8 o'clock in the morning and work until about 1 o'clock and he was not available to telephone or anything else then. In the afternoon he'd do his reading and whatever things came on. But he'd come down to lunch usually about 1 o'clock--a little after everybody else--and go to a certain table with some of his assistants and sit there. He didn't make much effort to mix with other people, but on some occasions when I did make it a point to sit down with him, I always had a very pleasant luncheon conversation and he was always very friendly.

One of Levene's early assistants, a physical chemist, Heimrod, lost the sight of both eyes--he was heating a solution, alkaline solution, and it spurted and got drops of alkaline in each eye. Levene was in the next room and ran in and washed his eyes out as quick as possible, took him over to a hospital, but the alkali penetrated one eye and he lost the sight in that rather soon. Alkali penetrates the tissues--you could get acid on your skin and in your eyes and it coagulates the tissues, but alkali just keeps eating in. And he lost the other eye a month later. Well, he was given a pension and he went over to Germany--he had taken his Ph.D. in Germany and most of his scientific friends were German, his father was German-born--so he went over there and lived the rest of his life. When I was over there in 1911, his father was Consul in Basel. And I heard that Heimrod was there visiting his father. So when I got through with my work in Berlin, on our way down to Italy we stopped off at Basel to see Heimrod and we met Carrel there! Carrel had left his island out in Brittany and gone to have a visit with Heimrod.

I heard that Carrel originally left France because he said apparently publicly that he did not know any explanation for some of the miracles at the Shrine at Lourdes where people went and got cured of their ills and threw away their crutches. That makes him persona non grata with the entire French medical profession. I don't know whether it was true or not--that's not official--but I heard that that was the reason why he got out of France.

Dr. O.: This would have been prior to coming to the United States?

Dr. V.: Yes. He was out of Chicago, I think, before he came to the Rockefeller.

Dr. O.: Yes. I seem to remember this, too; for a very brief period. How about Peyton Rous?

Dr. V.: Well, Peyton--his line of work was quite different from mine, of course. He was a very charming luncheon companion. If you sat next to Peyton you'd be sure that some really interesting topic would arise and that Peyton would make it interesting. And an awfully nice fellow. Very sincere. Hard working. The men that worked with him swore by him. He came to the Institute just about the same time I did, maybe a year later.

Dr. O.: The Rockefeller Institute certainly has made its mark in many ways. It's rather remarkable whey you look back at this period at the people that did work there at one time in different fields. Quite a collection of scientific talent.

Dr. V.: Yes, most of the senior men there were leaders in their fields. And a very large proportion of the junior men there went out and became leaders. It was Flexner's idea, when the Institute started, and which he told me when I went down from Ann Arbor to interview him, that young men would come there and work and give their enthusiasm and energy and learn from the older men and from the experience and go out after a longer or shorter time. And that was carried on. After I'd been in the Institute about three years, Carl Alsberg, who was at that time head of the Bureau of Chemistry in Washington, offered me the job of Assistant Chief which was rather an unusual thing for as young a chap as I was. I was very fond of Carl Alsberg--knew him very well. I went to Flexner and told him what the situation was and I said, "You told me when I came here that junior positions were temporary and that when good opportunities came on it was expected the young men would go out and start other things and it seems to me that this is the time for me to move on." He said, "No, some of our young men we want to keep. I'd like to have you stay on." So, otherwise I would have gone to the Department of Agriculture, but that's a typical Flexner decision.

Dr. O.: Right. Right, and brought on by your approaching him rather than his initiating it.

Dr. V.: Well, it only took him a minute to make up his mind! If I'd gone to Washington, I probably, to judge from other people, would have stayed there a few years and then taken a technical job in some food producing company, and been pretty rich! But Flexner--it was a critical moment and it didn't take him a minute to make up his mind what to do. And that was quite a commitment to make because it was a commitment.

Dr. O.: Yes. And from that point on does one just progress essentially in stages?

Dr. V.: It was years before I became a full member of the Institute.

Dr. O.: There were a limited number of full members?

Dr. V.: There was never a definite number, but the number was limited because each one meant practically a department and the Institute only had a certain amount of room. No, I was in no hurry to move up, but if I had to move out eventually, that looked like a good time and a chance to go with a man of whom I was very fond. No, I was in no hurry to leave Levene. I loved working with Levene.

Dr. O.: Are there any other members of the Rockefeller Institute or Hospital we haven't touched upon today that you would care to make a statement about or comment about in any way?

Dr. V.: Well, there was Alfred Cohn, who was a colleague in the Hospital all the time I was there. A profound scholar. Very sincere scientist. Good friend.

Dr. O.: And a brother of E. J.?

Dr. V.: A brother of Edwin, yes.

Dr. O.: Now, Edwin also had spent some time, did he not, at the Rockefeller?

Dr. V.: No, Edwin was never there.

Dr. O.: That's right. He and Dr. Hastings were first together at Columbia. I guess that was it.

Dr. V.: Edwin grew up pretty much under Henderson at Harvard, and stayed there and died there. But Alfred knew everything that there was known about the heart and circulation. He was a great scholar, and some of the men that worked with him went out and became leaders in clinical work on the heart. One of them was Robert Levy who was on the faculty at Columbia and was probably the leading heart specialist in New York. Another was Sam Levine.

Dr. O.: I'd forgotten that Sam Levine had spent time there.

Dr. V.: He just died this past year in Boston. He had a very eminent position in Boston.

Dr. O.: Oh yes. His son was a medical school classmate of mine.

Dr. V.: Yes?

Dr. O.: Yes. Herb Levine, who is now a cardiologist himself in Boston.

Dr. V.: I owed quite a good deal to a man that had worked with me for a number of years. That was Ed Stillman. He was a Hopkins graduate who had come up after he finished his internship at Hopkins, came up and joined the staff of the Rockfeller Hospital the same time that I moved into it. He was working with Allen on the diabetic patients and trying to do determinations of oxybutyric acid in urine by the methods that were available then and they weren't good and he had a devil of a time. Allen was a clinician and couldn't help him any in chemistry, so Stillman and I more or less teamed up to overcome his problems and eventually got working together very much. He took charge of patients whom we studied with regard to their acid-base balance and metabolism. He was a natural-born physician. He was completely interested in a patient, and in the whole patient, and I really learned a lot of internal medicine from Stillman.

Dr. O.: Edward Stillman?

Dr. V.: Edward Stillman, yes. He just died about a year ago. He eventually went with Palmer up to Presbyterian Hospital and was on the faculty there on a part time basis, and part time he practiced medicine--specializing particularly in metabolic diseases. He was a man, the kind of doctor that would make a patient think he felt better! One of our diabetic patients was a physician from Boston, Nathaniel Bowditch Potter; one of the old Boston families. Bowditch, you know, is an old Boston name. He was one of the leading physicians of Boston. Had everything behind him. Impressive, handsome fellow. Six feet tall, had a beard like Mephistopheles! A thoroughly good internist. He'd been a patient of Joslin and had been on the cream diet and been getting worse and worse and finally heard about the Institute and he came and put himself in our hands and Ed took charge of him. He had a tolerance of about 1600 calories. When he got down to that he didn't progress and he didn't get into trouble but he couldn't take more than that. He got in good enough condition to return to life. He was so much pleased with the way the Rockefeller Hospital went at things that he got some money donated and started the Santa Barbara Cottage Hospital out in Santa Barbara, California.

Dr. O.: Oh yes, I'm familiar with that institution. I had no idea that this name was connected with it though.

Dr. V.: He hoped to do the same sort of work and treatment that we were doing at the Rockefeller. Well, once in awhile he got low in his mind. He had had TB and he knew that the low-calorie diabetic diet involved a threat from the TB, but if he didn't stick to the diet his diabetes would progress (it was before insulin was available). When he really got discouraged he'd call up Ed Stillman, ostensibly to ask him about some perfectly trivial thing in his medication or treatment that he knew just as well as Ed did, but really just to hear Ed's voice over the telephone!

Dr. O.: That's remarkable.

Dr. V.: Ed makes me think of an old doctor that I met on a boat across the Pacific once. He said, "Really, the chief essential of a doctor is that the patient will do things to please his doctor that he won't do to save his own life!"

Dr. O.: It's very interesting, this, I'm sure, comes in not infrequently in the care of patients; somebody who can establish the kind of rapport that the patient feels this way.

Dr. V.: Well, Stillman was a real doctor. Stadie was another character that was a great fellow. I told you what a job he did on the oxygen chamber.

Dr. O.: Yes.

Dr. V.: He finished it and it was a complete job. Then he went on to other things, and other people took it up where he left off. I was surprised to find, and somewhat shocked, twenty years later, the young doctors that were using that oxygen chamber right there in the Rockefeller Hospital didn't know that Stadie had started it! He eventually went to the University of Pennsylvania as a Research Professor and did a great deal of work on carbohydrate metabolism, and, during the war, on the effects of high oxygen tension which became important with regard to divers. There was a great puzzle to find out why it is that high oxygen tension causes convulsions and is toxic in other ways. Stadie did a beautiful job in testing all the enzymes in the nervous system that you could think of and the effect of oxygen on them, but nobody yet has got the answer.

J. B. S. Haldane worked on it, too. He was the son of the John Scott Haldane I spoke of. They were a great family. Lord Haldane was John Scott's brother. Both Jack and his father didn't hesitate to use themselves as experimental animals. Jack, who was a big powerful fellow, put himself under high oxygen tension and had a convulsion which crushed a vertebra. He recovered from it so that all it left him with, so far as I know, was a stiff back. There's a story--I think it's printed in the Journal of Physiology--father and son were working on the effect of low oxygen and they had a chamber in which they could reduce the oxygen content by replacing it with nitrogen. Jack was in there making notes, and it was understood that when he felt the effects had gotten to the point where it was a good idea to stop it, he'd give the sign and the oxygen cock would be turned on. His father noted that Jack began to get blue in the face and had gone about far enough so he turned on the oxygen. Jack's note was: "Some bastard turned on the cock!" (Laughter) His father quoted that as evidence that Jack was using unusual language and Jack's friends said that it wasn't so unusual to Jack! He died in India. He was really one of the English geniuses, Jack was. He went into chemical genetics; almost a generation ahead of his time! I understood that he got out of England because it irked him to have American soldiers quartered there, and England becoming a base for foreign powers.

Dr. O.: Was this during World War II or after?

Dr. V.: It was after World War II.

Dr. O.: That's right. Now I'm putting this all together, yes, he was in India when he died.

Dr. V.: Everything that he published added something to whatever field it was in; it wasn't just some more work.

Dr. O.: This is a bit aside from what you've just been saying, but at the time, through the '20s and early '30s when you were doing this work at the Rockefeller, other than Henderson at Harvard, were there any other groups in the United States particularly or any other groups except possibly some of the Danes (though my immediate impression is that they came along a bit later) who were working in this general area?

Dr. V.: Well, the Danes had worked in it, there was Hasselbalch, and Lundsgaard had worked with Hasselbalch, and, after Hasselbalch, Erik Warburg. Haldane--J. S. Haldane--did a beautiful piece of work in showing that if you have reduced blood with a certain CO_2 tension and you run oxygen into it without changing the CO_2 tension, you push some of the CO_2 out of the blood. That is, as Hastings and I showed, the oxygenated hemoglobin is more acid than reduced hemoglobin so that oxygenating blood is like acidifying it. That's known as the Haldane effect, and it's very important.

With regard to the acid-base question, new techniques have been worked out for microdeterminations of CO_2 tension and pH in the blood, but the conceptions of respiratory alkalosis and acidosis and the metabolic acidosis and alkalosis--such as you have in diabetes--they are practically the same as they were when we worked on them at the Rockefeller. Astrup, in Copenhagen, worked out a beautiful little apparatus where with a few drops of blood you get CO_2 tension and pH. Interesting how he came to do that. He told me about it. They had an epidemic of poliomyelitis. There were a lot of children that got respiratory paralysis so they had to be kept alive by artificial respiration. And it was important to give them just enough respiration to keep the CO_2 tension and the blood pH within normal range. You could overdo it and give them respiratory alkalosis. Using my full-sized 50 ml. manometric machine which was what they had then, it took too much blood to do repeated determinations; they needed something you could do with a few drops of blood. For that reason Astrup worked out his micro machine which is very much used all around the world now.

Dr. O.: Yes. We had one in clinical pathology at NIH I know. Well the Danes, if you can make generalizations like this, certainly seem to be quite talented along the lines of developing techniques such as this, micromethods.

Dr. V.: Yes, the Danes have provided more than their share of good scientists. Linderstrøm-Lang developed a whole technique of ultramicrochemistry. And I think pretty near 100 Americans have gone through Linderstrøm-Lang's hands and come back and taken usually important positions. Hastings worked with him for awhile.

Dr. O.: Yes. Lowry-----

Dr. V.: Lowry and Anfinsen. Linderstrøm-Lang was a delightful person. I landed in Copenhagen one time twenty years ago and called him up and he said, "I'll be right over" and he came over to the hotel where we were staying and he had the oldest looking Ford jalopy that you ever saw in your life! Nobody would buy it for a secondhand car here, but we had a wonderful time. He not only was an elegant chemist but he also was a musician and he painted very well, and he was likely to be the life of any party that he was in.

His aim was to be able to follow what went on in a single cell and he worked out these ultramicromethods toward that. He did excellent work on chemical reactions, but he developed a whole microtechnique that is used the world around. He and Niels Bohr were the two great lights in Copenhagen for many years. Now they're both gone. Copenhagen is not the same town anymore. There are other outstanding scientists there, but it would be hard to replace those two.

Dr. O.: Yes. Craaford, the surgeon, is in Copenhagen, isn't he? Isn't he a Dane?

Dr. V.: Who?

Dr. O.: C-r-a-a-f-o-r-d?

Dr. V.: I don't happen to know him. I didn't get to know the surgeons in Denmark.

I was there once and I dropped in, as usual, to see Linderstrøm-Lang and he told me about the latest work they were doing and I told him what we were doing here at Brookhaven, and he said, "We have a little meeting after lunch once a week. Would you drop in and tell the staff about this work tomorrow?" I said, "All right." We had worked out quite a lot about the structure of the amino acid hydroxylysine that we discovered, and how it was formed by hydroxylation of lysine, and something about its function in collagen. He said, "Will you drop in tomorrow afternoon and tell the staff about it?" So I dropped in the next afternoon and instead of half a dozen young fellows he had a hundred people there and half a dozen full professors in the front row! I pretty near went through the floor because I was not prepared for such an audience.

Dr. O.: Oh my, it wasn't exactly what you were expecting!

Dr. V.: I hadn't prepared a formal talk.

It was too bad that Linderstrøm-Lang could not go on living. There are other good men in the Carlsberg laboratories still but they're not Linderstrøm-Lang!

[Pause]

Dr. O.: The date is May 28, 1969. We're again in the office of Dr. Van Slyke at Brookhaven National Laboratories. Prior to beginning a discussion of Dr. Van Slyke's career at Brookhaven, he's going to comment about Dr. William Mansfield Clark.

Dr. V.: I first met Clark at Woods Hole. We were both there as assistants to Dr. Carl Alsberg who was in charge of the Laboratory of Biochemistry at the Fish Commission Laboratory in Woods Hole. We had a very good time together and spent the summer there; that was in the summer of 1908. The summer of 1909, I went to Woods Hole and developed typhoid fever so I lost the first part of that summer!

Dr. O.: Was this a laboratory infection?

Dr. V.: No, it was an infection that came from a carrier in a dairy herd on Long Island and this dairy provided milk for the part of New York right around the Rockefeller Institute, and I presume that I picked it up at a restaurant there. There were, I think, about 80 cases from that one dairy. But I went back to Woods Hole for the summer in 1910. Alsberg had gone to Washington to become Chief of the Bureau of Chemistry at that time and so I succeeded to his place in charge of the laboratory, and Clark, who was one year my junior, became my assistant. There was no difference between us in actual experience or responsibility for the work, and we had a marvelous summer there together.

Dr. O.: He certainly had a very rich sense of humor.

Dr. V.: Yes, he had a great sense of humor. We used to work until 12 o'clock every morning. We were working on the metabolism of meat compared with fish, giving a meal to a dog every morning at 8 o'clock and catheterizing her at 4-hour intervals. After the 12 o'clock catheterization Clark and I would go for a swim and we'd take a nice long swim. The last hundred yards back we'd swim hard, and Clark always beat me by ten yards! He was a good swimmer.

Nineteen ten was the last year that I went to Woods Hole because in 1911 I went abroad and worked with Emil Fischer and I never got back to Woods Hole Laboratory again, but Clark and I always remained intimate friends, although we only occasionally would meet at my home or his, or at meetings, but we always felt as though we belonged to the same fraternity!

Dr. O.: His "Hydrogen Ions" became a classic in the field.

Dr. V.: Yes.

Dr. O.: Well, I can still remember, as a medical student, measuring the pH's of a variety of things using the old colorimetric methods.

Dr. V.: Yes. We didn't have the photometers then.

Dr. O.: Right, right. That's true.

Dr. V.: The two men that put pH on the map were Sorensen, in Denmark, and Clark in the United States.

Dr. O.: Again, in a sense, Clark's work, as your work in electrolyte balance and blood gasses, filled a void, really. It was an area of application in clinical medicine which has opened up totally new avenues.

Dr. V.: Yes, Clark's work was a great contribution.
[End of Side II, Reel 2]

[Side I, Reel 3] Recorded May 28, 1969.

Dr. O.: You had mentioned yesterday that it was 1949 that you left the Rockefeller, is that correct?

Dr. V.: Well, I reached the retiring age in 1948. From July 1, 1948 'til July 1, 1949, I divided my time between the Rockefeller and Brookhaven. I spent about half of the time at the Rockefeller finishing up work that I had going there, and half the time out here at Brookhaven getting the medical and biology departments organized. Then in the fall of '49, I moved out to Long Island and spent full time at Brookhaven from then on.

Dr. O.: Am I correct that the original thought behind the establishment of the Brookhaven National Laboratory was to make available to universities equipment which would be impractical for each to obtain.

Dr. V.: That was the idea behind it, yes.

Dr. O.: So the associated universities became an incorporated group. Is it five or nine--I can't remember the figure--universities involved in the associated universities.

Dr. V.: There were nine.

Dr. O.: Nine. With the idea of having one central facility which they would then share each-----

Dr. V.: Yes.

Dr. O.: -----and contribute to the support thereof, and so on. My impression is, and I think possibly on some of my conversations with Dr. Hastings, that early on in the planning of this there was some concern among people like Dr. Hastings that there was a move on, or at least initially the trend seemingly was toward limiting this facility to the physical sciences and not including medicine. Am I correct in this assumption?

Dr. V.: I was not in on the early planning. I think the Associated Universities, Incorporated was organized in '47 and the--or maybe a little before that--but in '48, when I was first in contact here, the laboratory was already going.

Dr. O.: I see.

Dr. V.: Phillip Morse, the physicist at Harvard, was the first Director.

He was Director then. He didn't like administrative work and rather soon he went back to Harvard and Hayworth took his place.

Dr. O.: Hayworth?

Dr. V.: Hayworth, yes. Leland Hayworth. The idea of having a laboratory at Brookhaven was generated by physicists and I imagine that you're probably correct in that they didn't think of having the life sciences as part of it at first. I don't know how the idea of the life sciences came into it.

Hastings was one of the first trustees. There were two trustees from each of these nine universities. The idea was to have one of the two who was a scientist and the other one who would be the administrator and that worked out pretty well. Well, Hastings was a scientist from Harvard and I presume he was one of the first trustees because he was a trustee when I was approached very early in 1948--the winter of 1948, as a matter of fact. Hastings talked to me first about it, then Morse came into New York and talked to me about it and then Shoup. At the start of Brookhaven the organization had two men that shared responsibilities, Shoup and Morse. I've forgotten exactly what Shoup's designation was but he eventually dropped out and was not replaced. I think it's always a mistake to have two heads to an organization.

Dr. O.: Actually, you came on then when Hayworth was here or was Morse here-----

Dr. V.: Morse was still on when I came on part time in July '48. When I came on full time in '49, Hayworth was Director.

Dr. O.: You came on with the title of Assistant Director with the responsibility for the departments of medicine and biology.

Dr. V.: Yes. I wouldn't be surprised if Hastings was responsible for medicine and biology being part of the plan. The idea of a Brookhaven, I think, definitely did originate with the physicists. There were other atomic energy laboratories at Oak Ridge and Argonne and Hanford, but in the northeast of the country where there was the greatest concentration of scientists, there was none.

Dr. O.: And the facility, originally, was literally using the buildings left over from Camp Yaphank which was rather rustic I'm sure for a period.

Dr. V.: Yes. They served pretty well.

Dr. O.: Some of them, I gather, are still standing over there by the apartments. Some of these long bungalow-type things on stilts that you described are still there.

Dr. V.: Yes. Some of them were turned into apartments and they were modernized so they made very comfortable apartments. The original medical department was in what was the old Army Hospital.

Dr. O.: I see. Then that has subsequently been torn down. This building I gather came----

Dr. V.: That's all gone now. It was about a mile and a half from here. It was over in the area where the apartments are, not very far from where you spent the night.

Dr. O.: Well, you started off with the idea of having a number of clinical beds to be used by the investigating group here at Brookhaven.

Dr. V.: Yes.

Dr. O.: Are the divisions now within the medical group essentially what they were at that time?

Dr. V.: They grew up as we got men here. When I came out here in '48 Dr. Robert Love, who is still here, and an assistant physician, who did physical examinations and took care of medical emergencies, were the only doctors in the medical department. Soon in 1948 after I joined the laboratory on part time I got Lee Farr to do likewise and together we recruited other men around whom research groups, which became called "Divisions" developed. Farr and I came here together on full time in 1949. The organization, you might say, grew like Topsy rather than being designed from the start.

Dr. O.: Built around the men.

Dr. V.: It was built around the men.

Dr. O.: The clinical beds you have here are primarily used for patients with malignancies that are receiving various sorts of radiotherapy or nuclear therapy?

Dr. V.: We have 48 beds and they're primarily for patients that are being investigated. If there is an emergency case--accident, for example, on the site--beds can be used temporarily to care for it, but their real use is for patients that are being investigated for the clinical conditions that they have.

Dr. O.: I believe you mentioned yesterday, you actually were even initially dividing your time between administration and your own laboratory work. How long did you stay in this position as Assistant Director for Medicine and Biology?

Dr. V.: I stayed in it for three years. By that time I had gotten Farr for Head of Medicine and Curtis for Head of Biology and the departments were well-founded and going and I considered that it wasn't necessary to have an administrator standing between the heads of these departments and Hayworth. I thought it was better to have Farr and Curtis report direct to Hayworth. Besides which, I liked the laboratory work more than administration! But we had a good start. We'd gotten what I consider top grade men to start, and if you start with top grade men you can keep it up; you set your standard.

Dr. O.: Are Dr. Farr and Curtis still at Brookhaven?

Dr. V.: No, Farr in 1961 accepted a call from Austin, Texas to organize a sort of "Brookhaven Medical Department" down there, and so he left and Bond, who was one of the men that he got who is both a Ph.D. and an M.D., was made Head of the Department. Bond had it for about five years and by that time Medicine and Biology had grown a good deal and the Director, Goldhaber, felt that he wanted to have an Assistant Director that could function the way I did, to advise him. So he stole Bond away from the Medical Department to be Associate Director and Dr. Eugene

Cronkhite accepted the Chairmanship of the Medical Department. In Farr, Bond and Cronkhite we've had three very superior men for heads of Medicine. We've been very fortunate to have been able to hold Bond and Cronkhite as long as we now have.

Dr. O.: When you returned to the laboratory, full time, or I should say really, when you came to Brookhaven initially because even then you had begun or continued working in the laboratory part time, what areas of research did you concentrate upon? Was there a change in direction from work you'd been doing at the Rockefeller Institute?

Dr. V.: Yes, quite. I'd been working on the kidney at the Rockefeller Institute. One of the things that was needed in isotope work, I remember Hastings said when we first talked, was an accurate and sensitive method for carbon 14. And I spent a couple of years working such a method out at Brookhaven with the help of Robert Steele and John Plazin. Organic substances were burned in two minutes with a combustion mixture of chromic and iodic acids. Then the CO_2 was transferred to alkali in the chamber of the manometric blood gas apparatus and CO_2 was determined the same way you do a blood CO_2. Finally the chamber was connected up with a gas-counting chamber, and the CO_2 was transferred to that and counted. That method is still a good deal used here in this laboratory; I don't know how much in others, but somewhat. That was quite a change from studies of nephritis. Then I also did some other work on methods and started work on the biological synthesis of collagen. The way I got into that problem was that while working in the Rockefeller Institute, Alma Hiller and I discovered a hitherto unknown amino acid, hydroxylysine, in collagen, and I was curious as to how it was formed, whether it was completely synthesized in the body or whether it was formed by adding oxygen to lysine. I had an assistant, Sinex, who came to me from Hastings' laboratory, and we worked on that and we found that the body could not make the hydroxylysine, or did not make it from anything except lysine. If we gave carbon 14 labeled lysine to a rat, we got carbon 14 labeled hydroxylysine incorporated into the collagen, with the same activity as the lysine that was also incorporated into the collagen. And furthermore, if we gave the rat hydroxylysine he couldn't put into the collagen-----

Dr. O.: In other words, he could not convert hydroxylysine to collagen.

Dr. V.: He couldn't use ready-made hydroxylysine. If it was already made for him he couldn't use it; he had to make it himself out of lysine in order to use it. It was also shown in work with Edwin Popenoe that the hydroxylation of lysine occurred at the moment of synthesis of the collagen. It was not a thing that went on for hours or days after the collagen was built, but hydroxylation of part of the lysine occurred during the putting together of the amino acids to make the collagen. Then the question arose as to the organic chemistry of the hydroxylation. That is, there are several ways which you can put an oxygen into a CH_2 to make a CHOH. One procedure that's used in living organisms a good deal is take away two hydrogens and form a double bond between two carbons. From a water molecule you put hydroxyl on one carbon and hydrogen on the other. That's known to occur in some biological reactions. We rather suspected it would be that. But that procedure would displace two hydrogens from two adjacent carbons on the 6-carbon lysine chain. That did not happen. There was only one hydrogen displaced, and that was from carbon 5, next to terminal carbon 6, which carries the NH_2 group. It was eventually found by studying the reaction with isotopes that an oxygen atom is taken on directly to carbon 5 of lysine and changes the CH_2 group to CH(OH), thereby changing lysine to hydroxylysine. In the meantime a group of investigators in Bethesda had been working on the hydroxylation of proline in the body to form hydroxyproline. The mechanism seems very similar to the hydroxylation of lysine, but there is one difference that has not been solved yet. When proline with a tritium atom on carbon 4 is hydroxylated the tritium is converted into tritiated water, THO. The enzymic action by which the hydroxylation is accomplished can be followed by measuring the tritium that is converted into THO. But in the hydroxylation of lysine, although tritium attached to carbon-5 disappears from the hydroxylysine, it does not reappear as THO. We can't find it in the water. That is one of the points we still have to work on. Another is to purify and characterize the enxyme that does the hydroxylation of lysine. Popenoe and Aronson are working on this problem.

Dr. O.: Have all of your studies, in general, been around collagen formation in recent years?

Dr. V.: I have done, as you might say, on the side, work in devising several methods, for calcium, lipids, and pH in plasma, for gasometric nitrate determination, and, with Aronson a method for measuring CO_2 in my gas machine and then transferring it to a scintillation vial for counting of carbon-14. But one might say that the main effort of the laboratory has been on the side of collagen.

Another problem concerning both collagen and hydroxylysine has been their reaction with periodate. The end of the hydroxylysine molecule has, on carbons 5 and 6, the structure $-CH(OH).CHNH_2$. When 2 adjacent carbons have one of them an amino group and the other a hydroxyl, the total group can react with periodate, splitting off the end carbon as formaldehyde and the amino group as ammonia. If, however, the amino group is bound, as by acetylation, or the hydroxyl group is bound, as by esterification, periodate does not attack the structure. The terminal group in hydroxylysine reacts with periodate completely and within a minute. When the periodate reaction is applied to collagen, however, the end groups of only part of the hydroxylysine react in this manner. If, after the reaction of collagen with periodate the collagen is hydrolyzed, we get back 50 to 90 percent of the hydroxylysine, depending on what kind of collagen it is. Only 10 to 50 percent is destroyed by periodate. It varies--you have acid-soluble, salt-soluble and insoluble collagens, and collagens from different animals. The non-reaction of part of the hydroxylysine in the collagens was a puzzle. Was the protein molecule so wound up that some of the end-groups of hydroxylysine were physically inaccessible? Or was either the amino or the hydroxyl group of part of the hydroxylysine bound in some organic combination, such as acetylation. Eventually it was shown in another laboratory that in the hydroxylysine residues that do not react with periodate the hydroxyl groups are bound by glycoside linkage to galactose, and that part of the galactose is also linked to glucose.

Dr. O.: The hydroxylysine with the glycoside linkage does not react with periodate.

Dr. V.: It was not a matter of the tertiary protein formation being one that made this part inaccessible, it was a covalent combination of the hydroxylysine hydroxyl with the sugar that made the hydroxylysine inert to periodate.

Dr. O.: I would imagine that some of the work done here on the Medical side is "basic science" and I imagine there is some similarity to the sort of experimental studies that are done in Biology. Is it based primarily on the interests of the men who happen to be there in those positions?

Dr. V.: Yes, that's also the situation in the Biology Department. At the start of the Brookhaven when I first came into it, there was a general question with regard to the policy of Brookhaven Laboratory whether the work here should be limited to work that involved atomic energy, radioactivity, etc.----

Dr. O.: Yes, that's an interesting point.

Dr. V.: That is, whether Brookhaven should do only work that could not be done anywhere else, or whether the field at Brookhaven should be general, but providing facilities that would make it possible to carry problems into paths that would be difficult to get into without the particular facilities here. That is, whether, for example, in a problem started in using atomic energy, if you got to a point where you didn't need atomic energy anymore you'd have to stop and say "I've got to quit." I was on the side that stood out for the broader policy and I think it became accepted that Brookhaven gives you special facilities but it doesn't force you to limit your problems to those that require such facilities. In all of this work, as a matter of fact, on hydroxylycine, almost all of it has been based on use of radioactive tracers. And in some of it this carbon 14 method that I spoke of, it has proved very useful.

Oh, our trouble in the Medical Department is to hang onto our good men. That happens to every productive laboratory.

Dr. O.: Certainly the physical plant here is so different from being in the midst of an urban center where you're hemmed in by the rapid pace, in a sense, by civilization. This is really like being out on a farm, literally. And you have everything you require, I'm sure, for your laboratory work right here. I would think perhaps the only shortcoming would be if an occasional wife would be upset at having to be so far removed from some of the conveniences of city life!

Dr. V.: Yes, I think that has happened, but it's not so far from New York that people can't go in for theater. When the Medical Department here was being organized there was quite strong pressure brought to have the Brookhaven Medical Department in New York City.

Dr. O.: For heaven's sake!

Dr. V.: Yes. The idea was that the Brookhaven Medical Department would be sort of a service department to laboratories and hospitals in the city and I stood out against that. I thought it ought to be here where it could utilize these unique facilities, and the association with chemists, physicists, and biologists of B.N.L., to produce original research.

Dr. O.: I was going to say, it would sort of defeat the purpose of having these unique facilities immediately available this way.

Dr. V.: Yes.

Dr. O.: I gather there are many graduate students from the Associated Universities and I guess from others too, who spend varying periods of time here working in different laboratories?

Dr. V.: Yes, particularly in the summertime. There has been a definite program of summer students coming out here, that is, up to this year. They are not only accepted, but their expenses are paid. It had to be cut down, at least in the Medical Department this year and I guess everywhere else, too, in Brookhaven because of the tight money.

Dr. O.: It's being felt throughout the government.

Dr. V.: I hope it won't last too long. We lost one of our good men, Katsianos, a chemist, that went to the new Mt. Sinai Medical School. We haven't got enough money to replace him. That is, there had to be a cost of living increase to other salaries and so forth so that although I think Brookhaven has been treated as well as any of the government laboratories, it hasn't been quite well enough to keep even. It's not a case of running to stay where you are, when you can't even run quite that fast.

Dr. O.: It's regrettable. I'm afraid it's going to get worse before it gets better unless something drastic happens as far as the financial commitments the country has.

Dr. V.: It's made worse by the inflation which originated in the previous financial administration of the country.

Dr. O.: Well, we certainly have ever since.

Dr. V.: It means that you have a continual upset of your equilibrium among different classes of people. I remember sitting next to the Vice-President of one of the big corporations. He was their economic adviser and he had followed the course of inflation in Germany after World War I--had been in Germany part of the time, and he said what happened was that the solid middle class had got wiped out. The very wealthy people were able to manipulate and dodge so that they hung on to what they had and ended up by owning everything! And the laboring class--they had to get enough to eat; they kept on getting that, their wages had to go up as the value of the mark went down, but it was a complete dislocation of the economy in that the people that were responsible for much of the prosperity of the country were eliminated.

Dr. O.: And this is what's happening here now.

Dr. V.: We're started in that direction.

Dr. O.: The growing discomfort and, I think, impatience of this class, this group, too, in our country is becoming more vocal certainly. Such groups forming as those refusing to pay their income tax until they close the loopholes for the very wealthy.

Dr. V.: I think this deficit philosophy is a vicious thing. I have never studied it but I can see the effects of it.

Dr. O.: We are seeing the effects of it, certainly.

Dr. V.: It amounts to running up debts for your successors to pay. What happened in Germany was this terrific dislocation and I think that Naziism was one of the results of it.

Dr. O.: Could well be.

You currently at Brookhaven are freed of administrative responsibilities and your time is devoted fully to the laboratory.

Dr. V.: Yes, the laboratory and writing of this book on manometric methods. Yes, I'm quite free from administrative work now.

Dr. O.: Which is as it should be I would think.

What goals do you have for the future other than completing this book? With such a fertile and profitable past what other things would you like to do, say on the completion of this book on manometric methods?

Dr. V.: Well, I would like to continue this work on collagen. It's the sort of thing that, like most research, you do it from step to step.

It's not a usual thing in research that you can tell several steps ahead what you're going to do-----

Dr. O.: No, of course not.

Dr. V.: -----because each step follows from the next one and I'd like to continue doing that as long as my intellectual and physical faculties hold up. When I feel they haven't why then I'll really retire. I've been very fortunate, physically, so far.

Dr. O.: As we were saying the other day, not on tape, you continue to play tennis quite regularly.

Dr. V.: I still play doubles.

Dr. O.: That's marvelous.

No, I suppose I asked that question thinking possibly other than the collagen work that you're doing, whether or not you had in the back of your mind, another area that you would like to attack.

Dr. V.: No, I haven't any plans to go into another field. If we ran out of problems on the collagen, there are enough other fields that I have been active in that I could take up again.

Dr. O.: Yes, that's true, that's true.

Dr. V.: The collagen work is really a continuation of work on amino acids that I began when I first went to the Rockefeller Institute with Levene. He put me to work on proteins. That was shortly after Fischer's ester method for isolating amino acids from hydrolyzed proteins had come out and we started working with that. Then we needed some method for following the hydrolysis of a protein; a method to determine either the carboxyl groups or the amino groups that are set free when the peptide links are broken. In an amusing way I came to work out the nitrous acid method to determine the amino groups. I had the general problem in the back of my mind--that was in 1910. I went up to Woods Hole to work in the Fish Commission laboratory during the summer, and came down with typhoid fever and was transferred to the Massachusetts General Hospital. They had some wards that were in little wooden buildings then.

Dr. O.: Oh, they still had the outbuildings for isolation and contagious cases?

Dr. V.: Yes, they said they then went back fifty years, those one-story wards. They were built at a time when the infectious theory of disease was first accepted. There was no known way to sterilize buildings and they were built with the deliberate idea that they would burn them down. Then it was found that you could sterilize them with sulphur dioxide and so forth, so they were still there and I was put in one of those wards. I got delirious, as is common in typhoid, and I still remember a peculiar experience. I was very hazy when I went in. I went up by rail with my wife from Woods Hole and walked in and was put to bed and I was very hazy for a day or two. Then one night just as it was getting dusk, my mind cleared up. I couldn't remember how I got where I was. I was in a room--it wasn't a very stylish room at all--it was very bare. It didn't look good! And I didn't feel good, and I was in bed but I couldn't see my clothes anywhere--"Where the devil am I and how did I get here?" And I figured I must have been foully dealt with and dragged some place, but why I wasn't killed while they were at it I didn't know. I lay there and speculated on it and a woman came in. She had a nurse's uniform on, but for some reason or other I doubted that she was a nurse. And I said, "Where am I?" She said, "Oh, be quiet, you have to be still." I said, "Well, I'd like to know where I am." She said, "You have to be still." That's all I could get out of her. Oh, and then she said, "You're in a hospital." Well, I was very skeptical about that and I said, "Well, if I'm in a hospital I'd like to see the intern who's in charge of me." "Oh, the intern can't be disturbed now; he's off duty." Well then I was damned sure that there was something phony about it. I waited until she went out and I got out of bed; I had only been sick a few days so I was still strong. I got out of bed and there was a window about six feet from the ground and it had a heavy screen on it and I hit that screen with my fist and tore it loose and was about to slip out of the window-----

Dr. O.: For heaven's sakes!

Dr. V.: -----when an orderly came in. He was a long, lanky Irish lad with red hair--I got to be good friends with him afterwards--and he had extraordinary presence of mind. He just slipped up behind me and put his arms around my chest--careful not to put them around my abdomen--and just hung on, he just hung on until I got tired of struggling and I gave up and got back into bed. He told me afterward that I so begged him to get me out of this dump, that he almost was in tears himself! But I've thought since that if the nurse had talked to me like a sensible being, that that wouldn't have happened.

Dr. O.: Given you some explanation.

Dr. V.: And it would be a good idea if more people knew that about handling people in delirium. They may not be completely crazy! Eventually, I was in the care of Dr. Richard Cabot, and I remember he came to my door and said, "You've got positive Widal; you're going to be here five weeks!" Five weeks from that day I was let out. I told my nurse that and she said, "Yes, it was kind of a joke the positive prognoses that Richard Cabot makes. We had a man come one day and wanted to be admitted and nobody could find what was the matter with him and they asked him why he wanted to be admitted and 'Well,' he said, 'just a year ago tomorrow Dr. Cabot said I had exactly one year to live!'" (Laughter) Cabot went into social service work later.

Dr. O.: He was rather a remarkable figure.

Dr. V.: Yes he was.

After I came out of the delirium and the fever went down, the last couple of weeks that I was there were terribly boring because I was not sick, but I wasn't permitted to get up--just had to lie there, and so I amused myself by thinking of whatever I could and I got to thinking about this problem of following protein hydrolysis by determining either the carboxyl or the amino groups. Well, in my work with Gomberg, I had done a great many diazotizations in synthesizing compounds, and it occurred to me that it might be possible you could diazotize aliphatic amino groups and split off the nitrogen the same as you could with aromatics and that that might answer the problem. My wife used to spend every day with me from nine to five and she'd write a postcard to my father telling him how I was. This idea came to me and one thing that lasted after the delirium was gone was that I had no memory! That is, I'd forget things in five minutes! My wife said if something struck me funny, I'd tell her the same story and she'd have to laugh at it ten times during the day!

Dr. O.: You had memory for distant past but not for the immediate past.

Dr. V.: Yes. Well, I was afraid I'd forget this idea, so as she was writing to my father and I said, "I've got an idea and I want you to take it down (she was a chemist so she could do it); I want you to take it down because I'm afraid I'll forget it." She said, "I'll write it." And she kept on writing and what she was writing was: "Don is better but he's still crazy in the head!" She didn't write it down at all. But it happened that I did remember it. And when I got back to the laboratory, I tried it out and after I got details worked out it became the nitrous acid method for determining amino acids. We used it among other things to demonstrate that free amino acids circulate in the blood and the amount that is taken up from the intestine during digestion is sufficient to account for all the nitrogen metabolism.

Dr. O.: It's remarkable how this ties back to your illness.

Dr. V.: But that was a funny way to get it. Yes, if I had stayed well and busy probably I might not have thought of it.

Dr. O.: A question that comes to mind which will be somewhat difficult to express and maybe something we will scratch out of the transcript, but being an "analytical chemist", I mean as a clinical biochemist, and having even at that point become involved somewhat with clinical biochemistry, when you were in the situation as a patient, did you have any thoughts about the practice of medicine as you saw it, in other words, as you were subjected to it as a patient? Perhaps with thoughts of some of these tremendous voids and things that were lacking. Really some of your later experimental work did fill a tremendous void which had great application in the practice of medicine. In other words, did you at any time find yourself, whether as a patient or under other circumstances, react to the way medicine was practiced in those days.

Dr. V.: Well, at the Rockefeller Hospital I think there was very close to an ideal point of view with regard to the handling of patients.

Dr. O.: Yes. But wasn't this perhaps unique in the sense that that isn't the way that medicine is really practiced throughout the country.

Dr. V.: I was chiefly concerned with learning as much of that procedure as I could and seeing the patients that were in my charge (because after I got into the kidney work the patients were really in my charge) were handled not only correctly but sympathetically. Occasionally I would know, as one does, of cases where the medical profession either in hospitals or in practice had distinctly lesser ideals. I don't remember that it occurred to me that the ideals of medicine, as they were at the Rockefeller under Dr. Cole, could be improved.

Dr. O.: No, I'm sure that's the case. I was thinking really more of your exposure to medicine as practiced in general at places other than the Rockefeller and not just the ethics or what-have-you, but actually the state of their knowledge--their scientific knowledge--which in so many cases, of course, was <u>not</u> what it was at the Rockefeller.

Dr. V.: I was always interested in that--both the ethics and the practice. I remember I was occasionally surprised by both what one might call the high degree of competence of practitioners--ordinary practitioners--and the opposite.

Dr. O.: The high degree of ignorance, too.

Dr. V.: The ethics--it's a good idea the public doesn't know the worst of it. Occasionally people would call me, somebody I knew would be in New York, and ask to be directed to a doctor. There was a distant cousin of mine from San Francisco--she was buyer in a big store there--came to New York-----

[End of Side I, Reel 3]

[Side 2, Reel 3] Recorded May 28, 1969.

Dr. V.: -----she called me and said that she had been pretty busy and had a lot of dinners in New York and she got to feeling uncomfortable and went to a doctor in the seventies on Park Avenue, which is a stylish medical part of New York, and he told her that she had to have two operations immediately and that they would cost her $1500 and he wanted her to be operated on the next day!

Dr. O.: Good God!

Dr. V.: That sort of took her breath away so she called me up. I sent her to a good practitioner I knew, and all she needed was a dose of Epsom salts!

Dr. O.: Unfortunately, this sort of thing still happens.

Dr. V.: Another thing. A man came to work with me from Chicago, he'd been an Assistant Professor there. His wife was also an M.D. and an Ann Arbor graduate--that was my own school. After they got married, in order to be in the same town with him, she took a job in a private hospital in Chicago. It was a hospital that so far as papers were concerned was in perfectly good standing. She found, after she'd been there long enough to see what was going on, patients who didn't need operations were referred by practitioners in Chicago. A case where an appendectomy, for example, would be referred for appendectomy, in that hospital they'd just slit the skin open and sew it up again and the patient would be let out and would think he'd made a very good recovery. When there was a really serious case, they were likely to get in trouble. It's a good thing the public doesn't know those things.

Dr. O.: Yes. Well, in this day and age, too, there's some element of informing them through some of these books that come out like <u>Intern</u> and <u>Doctor X</u>.

Dr. V.: On the other hand, in contrast, for several years when my children were very little--I had a boy and a girl--we spent the summer in a camp on Skaneateles Lake in the Finger Lake region of western New York, and one time when we got up there (my little girl was about four years old) I noticed the next day after we got there she went around pressing her throat. I took her temperature and she had a definite temperature. There was a local doctor there--it was just a little village--and I went up to get him and he came down, a man about forty, and he took a stick and looked in my daughter's throat and he said, "Doctor, I'd like to have you look at this." There was a membrane all over the tonsils. He said, "I know that the proper thing is to get a culture and make sure of this, but I have seen diphtheria before and I think that if you agree to it that we'd better start serum as soon as we can!" We were about 20 miles from Syracuse and I said, "Yes, of course." I figured it would be a case of going up to Syracuse to get the serum and he said, "I'll be right back." He got into his car and went up to his office and came back with some perfectly good brand new serum and he gave everybody in the camp (after testing everybody for sensitivity) an immunizing dose and a therapeutic dose for my daughter and in 24 hours the membrane was gone! I got acquainted with him. He used to come down occasionally and visit with me. He had an interesting history. His name was Twining.

Dr. O.: Twining?

Dr. V.: Twining. He was a nephew of Arthur Twining Hadley who had been President of Yale. He was graduated from the medical school in Buffalo, and he came to this place which was called Borodino from the place where Napoleon fought the Russians. He came to this place to take practice during the summer of an old physician who wanted to rest. That was just after Twining had his internship, and the old physician never came back! Twining liked to hunt and fish and it was right on Skaneateles Lake and the people there were old-time American stock. He got to know the local people and to like them and so he stayed on to take care of them and ended up by marrying one of the local girls and staying there for good! He used to go to Syracuse Medical School for a refresher course so he kept up to date. And he was an efficient, dedicated family doctor. Thank God, his ideal is the rule and not the exception.

Dr. O.: We might just say, for the record, I know we were speaking of your son, Karl Keller, who is now a surgeon in practice in the Nassau Hospital in Mineola on Long Island. And your daughter?

Dr. V.: Daughter? She's a secretary with the Du Pont's in Wilmington. She's been with them for twenty-five years. The Du Pont Company treats its employees very well.

Dr. O.: I noticed that you've had the unique experience, and I'm sure pleasure, of publishing a paper with both your father and also with your son, which I think is quite unique in the annals of medicine and science.

Dr. V.: Yes, the first piece of work that I published, as a matter of fact, was published before my thesis got out that I did with Gomberg; the first work was done with my father. He was an expert on the chemistry of milk and he was interested in and did quite a good deal of work on casein. He was working with one of his assistants, Ed Hart, who afterwards became Professor of Agricultural Chemistry in Wisconsin. They found when casein was precipitated with acid that some of the acid stuck to the casein precipitate. Also if the precipitated casein was washed with water until the water was neutral and then shaken with dilute acid it would combine with some of the acid. The question was: What was the nature of the combination? Was it physical or chemical? I had been taking physical chemistry at Michigan. I had a very good teacher of physical chemistry, Professor G. A. Hewlett. He was a pupil of Ostwald. He was about 30 then and full of enthusiasm, and I took all the physical chemistry that was given. Hewlett was a marvelous teacher. If I went to him with a question, his answer would be to give me a reference in the literature and if I couldn't understand it he'd help me work it out. I joined father on the casein problem during the summer vacation of 1906. We were able to show that casein took up acid by a process that had the characteristics of physical absorption. The acid was not taken up in the way that it would behave if it were a chemical combination. Greatly different amounts of different acids were taken up, without relation to their strength as acids. I measured the amounts that were taken up by doing conductivities on the supernatants which gave a very sensitive measure. The procedure delighted my father, who had grown up before conductivities were done.

Dr. O.: You were still in college at the time. This was during summer vacation?

Dr. V.: I was still in college. This was the year before my final year at Ann Arbor. My fiancée had no mother or established home, so my people invited her out to spend the summer and, as I have said, she had been taking a chemistry course at Ann Arbor. She joined the work on the problem; my younger brother, who was a pretty good mathematician, did the calculations.

Dr. O.: For heaven's sakes, it was really a family production!

Dr. V.: My father had a house on the Experiment Station site--it was right across the road from the laboratory and we'd get things started at 7 o'clock in the morning, then I'd go back home and have breakfast. We'd keep experiments going until suppertime. After supper we'd play tennis. In the course of the summer, we got a job done that would ordinarily have taken a year, and it was accepted by the <u>American Chemical Journal</u> which was the best journal we had then. That was published by Ira Remsen, of Johns Hopkins. The American Chemical Society had begun to publish its journal but Remsen's journal was the most respectable chemical journal we had in America then.

Dr. O.: As I remember, Ira Remsen, upon the opening of the Medical School at Hopkins, taught the course in chemistry for medical students and then they finally got----oh dear, the man that Clark followed. His name slips me at the moment--the first Professor of Chemistry at the Medical School.

Dr. V.: Remsen was one of the Americans who went to Germany in the late 1800s and brought German science back to this country. He was a great teacher. He came to Ann Arbor and gave the commencement address one time while I was there. I remember very few of the speakers that I've heard in my lifetime, as one does, but I remember Remsen. He became President of Hopkins. He intended to continue his scientific work, but he found it was impossible. Most people who have tried to combine that extent of executive work with research find it an impossible thing. If you're an executive you belong to the people that work with you. If anybody can say "he's my chief" that's a real possessive, he owns you! The popular idea may be that the chief possesses his subordinates; really they possess the chief! They have a right to access to him and to his time and to demand his help and that has priority over any private projects that he may like to carry out.

Dr. O.: You know this is the deciding factor I'm sure, for many people, the age-old problem of the competent scientist who has made a name for himself and contributed to the field, then the next stepping stone in so many people's eyes is to make him Chairman of a department and then more administrative work and so on, it removes him from his bench.

Dr. V.: If he has very good subordinates that he can keep with him, he can keep going for awhile by working by proxy, and that's not likely to last.

Dr. O.: I think it's very interesting. One of the things that was so obvious was Dr. Hastings' tremendous delight at getting back to the bench when he left Harvard and getting to Scripps. He was like a kid! Just bubbling over with joy at getting his hands on the instruments again.

Dr. V.: Yes, he loved Harvard and Margaret loved the social side there, but the chance of getting away from administrative work and back to the laboratory tempted him to go to La Jolla and I don't think he ever regretted it. He liked to teach, he liked to teach; he said it was a continual stimulus to be in contact with those very fine young minds. Of course, the Harvard medical students were a highly selected bunch, the same as the Hopkins ones. There was great difference between Harvard College and the Harvard Medical School in the relation of the students to each other.

Dr. O.: That's very interesting.

Dr. V.: My son went through the college and the medical school both at Harvard. The students in the college had not been related to each other like comrades at all; they were more like people living in apartment houses in a big city. Harvard tried to overcome it. In order to do that, the system of houses for the students to live in during their last three years of college was devised. Each house had a couple of hundred students and a housemaster, and the students were supposed to get on a first name basis with each other. The freshmen were all put in the Yard. A large part of the freshman class were boys from prep schools in New England, where, if you were wise, you sent your son in case you wanted him to get into Harvard and last through the first year. Harvard College took in 1200 freshmen and dropped 400 of them.

Dr. O.: Good Lord! I had never realized that.

Dr. V.: Yes, that was their policy. And in order to stick you had to be in the upper two-thirds. Well, these prep schools trained their boys to meet the situation. Their teachers knew exactly what their students would get every day at Harvard in their freshman year. They trained them to get into that first two-thirds. If a boy came from even a very good public school--my boy came from the Bronxville High School, which was a very good high school--they were at a disadvantage in competing with the prep school boys. The high school boys and the prep school boys never did mix very much. Kell and two other boys that went from Bronxville had an apartment on the top floor of one of the houses in the Yard and there was another apartment for three boys on the other side. They didn't speak to each other for about six weeks and then they got together because it was advantageous to get a telephone out in the hall between them, and they found they liked each other. But it apparently wasn't the thing to do to force yourself on anybody else. Then the second year, Kell was in one of the houses and it wasn't any better. He said if you go down and sit next to another boy and you asked him to pass the salt, he'd pass it but it didn't mean that you became acquainted with each other.

As soon as Kell got into medical school it was completely changed; the Medical School was like one big fraternity. He moved into Vanderbilt Hall and while he was still moving in some of the upper classmen came in and introduced themselves and said that they would be glad to help in any way they could. And from that time it was a different school.

Dr. O.: It is a contrast. I know when you started, I thought well, I experienced something like this myself, I suppose, at two totally different institutions. At least the camaradarie and the long-standing friendships one made in medical school are far greater than college. But this is very unique, I think, in a sense at the same institution to have a contrast like that.

Dr. V.: I don't know whether Harvard is unique.

Dr. O.: I shouldn't say unique to Harvard, but possibly more characteristic of some of the Ivy League schools where you have a number of fellows from prep schools who have known each other through prep school and still remain a clique, in a sense, when they get to college.

Dr. V.: That was completely different from anything that I knew in Ann Arbor.

Dr. O.: I'm sure.

Dr. V.: The Midwest is different. If I was in a class there with another fellow and somebody asked me if I knew him, I'd say yes, of course I was in a class with him. It was a peculiar situation in Harvard College; nobody liked it.

Dr. O.: And yet they wouldn't take steps to change it.

Dr. V.: Steps were taken but they didn't work. It was just the inertia was so great. I don't know any other word to express it. It was just a very peculiar psychological phenomenon.

Dr. O.: Was Dr. Hastings son in your son's class?

Dr. V.: Hastings' son you say? No, he was younger; quite a bit younger. Young Hastings is doing just what he loves now. He's a Professor of Music at Trinity College. He had a most extraordinary mind. I remember when he was about twelve years old I visited Hastings in Chicago, and the young Baird had just written a thesis on the Supreme Court--part of his English course. I read it and it was the most illuminating description of the role that the Supreme Court had played in the development of our working constitution that I read anywhere.

Dr. O.: At the age of twelve!

Dr. V.: Yes, at the age of twelve. He could have been a quiz kid because he could tell you most any historical date and the circumstances around it that you might ask for. When he got interested in music he had the same type of encyclopedic memory for anything in music. He'd put a record on and before he'd heard three bars he'd know what it was and probably could tell you what orchestra played it. But he didn't like science.

Dr. O.: No, I gathered he sort of followed Mrs. Hastings' fondness for art and music and so on.

Dr. V.: May I ask how it came to----you took this work in medical history?

Dr. O.: Well, it started off as a hobby. I found myself spending all of my spare time reading and writing in the history of medicine. This began while I was a surgical resident and by the time I completed five years of surgical training and gone into pathology, I essentially spent all of my spare time in this manner. I didn't write any scientific papers at all while I was a pathologist. Everything I wrote was in medical history. My chief at that time was quite sympathetic to this; he thought it was fine. And the opportunity came to go to the Library. I was literally finishing up my residency in pathology at NIH and got a phone call from the Director of the Library who said "I understand you're interested in medical history and the problems of biomedical communication?" and I said, "Yes." I went over and had lunch and that was in July or prior to July, of 1964 which is when I went to the Library. After one year, I was full time in the history of medicine; thoroughly enjoyed it, I really have.

Dr. V.: Yes. Well, I can understand it. I am fascinated by history myself, but I never had time to spend on it that I'd like to.

Tell me, do you think medicine made any progress at all during the centuries after the Roman Empire broke up?

Dr. O.: Until the Renaissance you mean, in other words through the medieval period?

Dr. V.: Yes.

Dr. O.: Well, it's generally looked upon as being a period of some stagnation and the period where the records of the past were passed along practically unchanged with very slight modification, by the succeeding many generations and the chroniclers of medicine, as it were, in the religious institutions of the day.

Dr. V.: Practically everything was carried on through the Church, wasn't it? The monks were the only people that knew how to read!

Dr. O.: Yes. It was the big problem. They were the people who literally preserved, in a sense, the western heritage. And, in time, again things started out to blossom out in new directions, oftentimes at a level far below the educated man with your barber surgeons and what-have-you. It took many, many years for them to become respectable and medicine was quite pompous and very stilted in its ways and the educated physician really was not very well-educated in medicine at all. Whereas your uneducated man who was treating patients in the small communities was learning a good deal more medicine, but he was not recognized by the academicians. It took quite some while for this to mold into one.

Dr. V.: Dr. Cole was very much interested in medical history--I think particularly in the development of medicine when it was coming out of the dark ages. I remember his quoting an Italian Florentine, I think it was Redi.

Dr. O.: Francesco Redi?

Dr. V.: Yes.

Dr. O.: Spontaneous generation.

Dr. V.: Redi said the difference between no physician and a good physician is not great but the difference between no physcian and a bad physician is very great! Redi wrote a famous poem in praise of wine, I think. It took a long time for the doctrine of laudable pus to disappear.

Dr. O.: Oh yes. Yes, in my work on Dr. Halsted, reviewing the status of surgery in the late 19th century and early 20th century, it's remarkable to see the steps that were taken and how this was approached--the fact that there were surgeons who wore gloves between operations but not at surgery.

Dr. V.: Yes?

Dr. O.: Yes. There were some who said you should keep your hands protected to keep them clean so that when you come to operate, you see, you haven't exposed them to all these things. Then there were those who used just finger cots to protect themselves, you see, from contamination. And Dr. Halsted himself who is given credit for introducing rubber gloves into general use in surgery by all members of the team did not introduce gloves as an aseptic method at all. It was simply that his scrub nurse had developed a tremendous skin reaction to the mercuric chloride so he approached the Goodyear Rubber Company to see if they'd make a pair of thin rubber gauntlets which she would wear when she picked the instruments up out of the basin of mercuric chloride and passed them on to the next man in line. After awhile his fingers started to bother him so he just started wearing the gloves to protect his hands from this stuff.

Dr. V.: That's interesting.

Dr. O.: And it wasn't until Joseph Bloodgood, who was one of Halsted's residents, some four years later started to routinely wear them for aseptic purposes in the operating room.

Dr. V.: Well, I suppose they would have been impractical unless they could have been made very thin because a surgeon depends on touch so much.

Dr. O.: Well, this held it back for some while. Many surgeons refused to wear them for this reason, that was the argument, that they had to have their sense of touch. Some would take the glove off and stick their hand in the wound, feel it and then put the glove back on. Others used very fine cotton and linen gloves. They felt they could feel better through these without the tension of the rubber glove on their hand.

Dr. V.: I guess all pathologists wear gloves when they do an autopsy now, don't they?

Dr. O.: To my knowledge, yes. Yes, I'd say so. Again, there are perhaps some senior members who-----

Dr. V.: ----thought it wasn't quite masculine.

Dr. O.: -----yes, would come in and not bother to put on a glove just to handle some tissues or something you were showing them, but I think they all do now.

One of the two senior residents in surgery when I was an intern at Hopkins was operating on a TB case and they were working down in the chest.

They were doing a pulmonary resection and the assistant resident, quite by accident, working in a field where the visibility wasn't too good was taking a Kocher clamp to clamp a bronchus and he got this chap's finger and he got a soft-tissue tuberculous infection. It kept him from operating for four months of his twelve months of residency--four months or more. He couldn't go in the operating room.

Dr. V.: Did they save the finger?

Dr. O.: Oh yes. Saved the finger and it finally cleared up, but it came at a rather bad time because it interrupted the--that's the one year, of course, in the seven-year residencies when you're really able to carry on a lot of surgery because in that pyramid system they have at Hopkins you start off doing absolutely nothing as an intern there. If you make a move even to pick up the suture to hand the resident, the assistant resident whacks your hand; you just stand there with the scissors and cut it once it's been tied. You don't take that next step. So you have to wait awhile before you do much surgery.

Dr. V.: A lot of pathologists have picked up TB, and that's a shame.

Dr. O.: Because oftentimes it's clinically not suspected and you'll get in the autopsy room and not be wearing a mask--you'll be in a gown and gloves.

Dr. V.: One of my son's classmates who went into pathology got TB; he got over it, got it arrested. But it took him some time to get it arrested.

Dr. O.: Oh, it's still a prevalent disease, there's no question of that.

Dr. V.: But people now don't realize what a scourge tuberculosis used to be. And I don't know that it's certain altogether why it has diminished so much.

Dr. O.: To some degree, I suppose, earlier detection plus in general better health conditions.

Dr. V.: General conditions are better; as far as I know that's about all one can say.

Dr. O.: It's still very prevalent, certainly in the low income groups.

[Pause - Tape off]

Dr. V.: The Eli Lilly Pharmaceutical Company, I think, was very generous in their support of basic science. I served as adviser in the distribution of about four hundred thousand dollars a year for five years. I visited colleagues in universities in this country and Europe, and made reports to Lilly. I think that 90 percent of the recommendations I made were honored by the Lilly people.

Dr. O.: (Examining some notebooks of Dr. Van Slyke) Are these more or less notebooks of your impressions of these various departments and what-have-you and what was going on in science in these various areas?

Dr. V.: Those are the little books. Yes, they're notes of interviews

I had with people and dates that I made in my work for Lilly. It was very interesting. I spent two or three months each year traveling for Lilly between 1951 and 1956.

The Lilly's were very nice people to work with. I said I didn't care to travel without my wife and they appointed her as my traveling secretary, and she was a godsend. She's Danish and familiar with continental people and when I'd been talking with colleagues all day long and then we'd be at a dinner, thank God she could take over.

Dr. O.: That is a godsend!

Dr. V.: When we were on our way out to Taiwan in '61, our travel agency forgot to get visas so we stopped on the way out at Tokyo and I was warned that I'd have trouble getting transportation from Japan to Taiwan if I didn't have a visa. So I went around to the Chinese consulate and the man there said that they'd have to consult with Taiwan and it would take several days. Well, I was due to leave the next day. By good luck, I had a letter from the Chinese Surgeon-General in my pocket. He'd written welcoming us to Taiwan. I drew that out and turned it over to the consulate and he went out in the other room and came back all smiles and welcome and said everything was OK.

Dr. O.: That's very interesting. Was this unique, you think, to this particular time or is it always that way as far as getting into Taiwan.

Dr. V.: I don't think it was unique for that time. I think it is part of the defense of Taiwan against Communist infiltration, but they're very careful who comes in from Japan, because the Communists from the mainland could come in that way and the Taiwan government doesn't want to have any unnecessary trouble that might be imported that way. They haven't had any youth revolt in Taiwan. They have very high standards in their schools there. Phillips' children--at least some of his children--went to Chinese schools and they progressed, as nearly as I could make out from their mathematics, somewhat faster than our children do. They work six days a week. They don't have Saturdays off, and if they've had difficulties they can see their teachers on Sunday to get caught up. And only the upper 10 percent can go to college and only a very small percentage of those can go to medical school.

Dr. O.: It's quite a contrast to some other situations, isn't it?

Dr. V.: Yes, I think that Phillips' daughter going to a Chinese school there was better taught than she would be going to many of the high schools in this country. We're not going to stay ahead of Asia indefinitely!

Dr. O.: I believe it was Dr. Hastings who had mentioned that they were told by one of the academicians in Taiwan that they were not giving any advanced degrees--I don't know if this was in biochemistry or just what subject--until they felt that the quality of their teaching and faculty and so on was able to match any western colleges. In other words, they weren't diploma mills by any matter of means. They were fully cognizant of the needs of higher education.

Dr. V.: No, they recognized the desirability of standards. They're doing work that's considered sound in the new nuclear plant in Taiwan. Some excellent Chinese advanced students have come over to this country to get educated to go back. The American Bureau for Medical Aid to China for a good many years has had several fellows each year in this country--some of them faculty members, some of them younger men that were faculty timber. I think there's only one that hasn't gone back. They could stick to this country and get better jobs and better facilities in which to work.

Dr. O.: It's interesting so many have gone back and this may again be characteristic. This is a contrast to some of the other countries where it's a serious problem, people coming over here in science and medicine and staying.

Dr. V.: The Rockefeller Foundation has had that problem with European Fellows. I've talked with Foundation Directors about it. They put all the pressure they can on and they have agreements that these boys would go back to their own countries, but they don't always hold.

Dr. O.: And I guess when the chips are down there's not a great deal they can do to force them.

Dr. V.: Some of them were justified in staying because of conditions at home. There were two Spaniards that came over to the Rockefeller Institute from Barcelona before the Revolution in Spain. Then the Revolution broke out and the Institute they were to go back to just didn't get going. So they stayed on. One of them married my wife's daughter. Jordi Casals, a virologist. He gave the Theobald Smith

Lecture a couple of weeks ago on virology at the Rockefeller Institute. He's with the Rockefeller Foundation and also has a professorship at Yale. And the other one was Jordi Folch who came to work with me for a year and then the revolution broke out so he couldn't go back. He came on a Rockefeller Foundation Fellowship and he took hold so well that he was appointed a regular assistantship with a salary and stayed with me seven years. Then he became head of the McLean Hospital laboratory which is connected with Harvard, and he's still there. He's a Harvard professor.

[End of Side II, Reel 3]

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