CHEMICAL HERITAGE FOUNDATION

MILDRED COHN

Transcript of Interviews
Conducted by

Leon Gortler

at

University of Pennsylvania

on

15 December 1987 and 6 January 1988

(With Subsequent Corrections and Additions)

THE BECKMAN CENTER FOR THE HISTORY OF CHEMISTRY
Oral History Program

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Dr. Mildred Cohn

(Date) March 10, 1993

(Revised 20 February 1989)

> Mildred Cohn, interview by Leon Gortler at the University of Pennsylvania, Philadelphia, Pennsylvania, 15 December 1987 and 6 January 1988 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0080).

Chemical Heritage Foundation
Oral History Program
315 Chestnut Street
Philadelphia, Pennsylvania 19106

MILDRED COHN

1913	Born in New York, New York on 12 July

Education

1931	B.A., chemistry, Hunter College
1932	M.S., chemistry, Columbia University
1938	Ph.D., chemistry, Columbia University

Professional Experience

1932-1934	National Advisory Committee for Aeronautics
1937-1938	Research Associate in Biochemistry, George Washington University School of Medicine, Washington, D.C.
1938-1946	Research Associate in Biochemistry, Cornell University, Medical College, New York, New York
	Washington University, Medical School, St. Louis, Missouri
1946-1958	Research Associate in Biochemistry
1958-1960	Associate Professor of Biochemistry
1950-1951	Research Associate, Harvard University Medical School
	University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania
1960-1961	Associate Professor of Biophysics and Physical Biochemistry
1961-1978	Professor of Biophysics and Physical Biochemistry
1978-1982	Benjamin Rush Professor of Physiological Chemistry
1982-	Benjamin Rush Professor of Physiological Chemistry, Emeritus
1982-1985	Senior Member, Institute for Cancer Research, Fox Chase, Philadelphia, Pennsylvania

Honors

1952-1958	Established Investigator, American Heart Association
1963	Garvan Medal, American Chemical Society
1964-1978	Career Investigator, American Heart Association
1971	National Academy of Sciences
1972	American Philosophical Society
1975	Sc.D., Medical College of Pennsylvania
1975	Cresson Medal, Franklin Institute

1977	American Academy of Arts and Sciences
1977	Foreign Member, Institut de Biologie physico-chimique, Paris, France
1978	Sc.D., Radcliffe College
1979	Award, International Organization of Women Biochemists
1980	Award, U.S. Senior Scientist, Humboldt Foundation, Federal Republic of Germany
1981	Sc.D., Washington University, St. Louis
1981	Chancellor's Distinguished Visiting Professorship, University of California, Berkeley
1982	National Medal of Science
1984	Sc.D., University of Pennsylvania
1984	Sc.D., Brandeis University
1984	Sc.D., Hunter College
1984	Award, American Academy of Achievement
1985	Sc.D., University of North Carolina
1985-	Visiting Professor of Biological Chemistry, Johns Hopkins University School of Medicine
1986	Chandler Medal, Columbia University
1987	Distinguished Service Award, College of Physicians, Philadelphia
1988	Honorary National Member, Iota Sigma Pi
1988	Remsen Award, Maryland Section, American Chemical Society
1988	Ph.D. (honorary), Weizmann Institute of Science, Israel
1990	Sc.D., University of Miami

ABSTRACT

Mildred Cohn begins the interview by reflecting on her childhood, education, and family life, describing how she was prepared to enter college by age fourteen. She then discusses her undergraduate experience at Hunter College, recalling the difficulties she encountered as a woman in the sciences. She continues by recounting her graduate years at Columbia, where, after working for a short time at the National Advisory Committee for Aeronautics, she began her work with isotopes in Urey's lab. She tells of her experience working with du Vigneaud at George Washington and Cornell universities and contrasts it with the much more independent atmosphere of the Coris' lab at Washington University in St. Louis. Finally she describes her years at the University of Pennsylvania and highlights the most fulfilling aspects of her work. She concludes with her analysis of the future of biochemistry and advice for those, especially women, interested in pursuing a career in the natural sciences.

INTERVIEWER

Leon Gortler is professor of chemistry at Brooklyn College of the City University of New York. He holds A.B. and M.S. degrees from the University of Chicago, and a Ph.D. from Harvard University. He has long been interested in the history of chemistry, and helped establish the Beckman Center's oral history program. He has conducted over forty oral and videotaped interviews with major American scientists.

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INTERVIEWEE: Mildred Cohn
INTERVIEWER: Leon Gortler
LOCATION: University of Pennsylvania
DATE: 15 December 1987

GORTLER: I know you were born in New York on 12 July 1913, but I know almost nothing else about your early life. Can you tell me a little bit about your family? Start with your parents; tell me their names and what they did.

COHN: My father's name was Isidore M. Cohn and my mother's maiden name was Klein. Her first name was Bertha. My father was a renegade rabbi. He left Russia about 1906 or 1907 (it was soon after the unsuccessful revolution of 1905) for two reasons; one, he was about to be ordained and he didn't want to be a rabbi, and the other was that he was twenty-one and would have to enter the Czar's army which he didn't want to do either. So for both those reasons he left and came to this country.

My mother came about the same time. I don't know the exact date, but about the same time. They knew each other in Europe. They were childhood sweethearts and eventually married each other. Like all immigrant girls she went to work in the needle trade. She thought she'd rather die than do that after a while! Happily she got married, so it was no longer a problem for her.

My father also went into the needle trade and he was terrible at it. He knew how to do nothing manually, nothing practical. He seemed to have no manual dexterity. He was employed as a cutter for trousers and he couldn't do it, so he invented a machine to do it. His boss was so impressed with him that he took him in as a partner, though he had no money to invest. My father was always too imaginative to stick to small business, so after a while, he expanded. They bought a factory in Pennsylvania and then they had outlet stores. Well, to make a long story short, they went bankrupt. They paid off everyone with the result that my father was penniless again. Then he went into the linotype business of which he knew nothing, but he learned it very quickly.

My father once told me that there was a friend he had in Europe who asked him to write his impression of this country. And my father, who never wrote a letter longer than five lines, after a month or two in the U.S. wrote his friend a fourteen-page letter and told him not to come. He was so disillusioned when he first came to this country.

I had a brother, Albert, who was two years older than I. He eventually became a lawyer. This disappointed my father greatly. He wanted a son who had a Ph.D. in philosophy, not a son who had a law degree. He thought that was not scholarly enough.

I guess I became interested in chemistry because I had a very close friend through grade school and junior high school whose father had several beauty salons and, on the side, used to manufacture beauty products. He told both of us that chemistry was a wonderful career for women to go into. I remember that very well. As a matter of fact, she became a chemist too.

GORTLER: What was her name?

COHN: Her name was Euterpe Martin. I've often wondered what happened to her. I haven't seen her since my high school days. By the time I got to college, I wasn't at all sure that I wanted to be a chemist. I was so interested in everything that I studied that I had a hard time deciding. But then I suppose I was a bit on the arrogant side. I decided I could learn everything else by myself, but science I'd have to study at school.

GORTLER: How about before you got to college? Let's go back and talk a little bit about your earlier schooling.

COHN: Well, I was a very bright little girl, I suppose. Also the schools were very crowded so they let me skip all the time. I graduated from high school when I was fourteen.

GORTLER: Yes, I did some calculations this morning and I decided you must have entered college when you were about fourteen.

COHN: That's right. I did. I went through, skipping grades, rapid advance, and so on in grade school and junior high school. And I never had any academic problems; I was a good student. I was a good little girl too, though I must say some of the things that happened there were quite corrupting morally, in my opinion. But that's beside the point. That had nothing to do with my later career.

GORTLER: Were there any teachers during high school or junior high school that were particularly influential? Anything you read during that period?

COHN: Well, let me tell you about high school. I took two years of chemistry in high school.

GORTLER: That was rather rare at that time.

COHN: Yes, it was. But there was a chemistry teacher who was very enthusiastic. I think his name was Fierwasser. After giving the usual course in chemistry, any student who wanted to study more advanced chemistry could take a second year. And I did. I also was a very good mathematics student in high school. I was on the math team, needless to say, the only girl on the math team. In general, I sort of enjoyed myself in high school although, of course, I was much younger than most of my classmates. Consequently, I had very little social life with my fellow students. But I had a great deal of social life at home. My father was a Yiddishist--a Yiddishist is a person who is interested in perpetuating Yiddish culture. These people had a cooperative housing project in the Bronx which was called the Yiddishe Cooperativa Heim Gesellschaft, and that's where I grew up. We moved there when I was about thirteen. We had all kinds of activities, cultural activities. You know, everyone had a little Mischa or a Sasha who either played the violin or painted. And we had clubs of all kinds. I remember when I was fourteen being in a play by Eugene O'Neill. All my social life was centered in the community, not at school.

At college I started taking chemistry in the second semester of my freshman year. First of all, I should tell you that I was very disappointed in college. In high school, they used to divide us into thirds depending on ability; the top third, the middle third and the lowest third in each subject. And I was with very bright kids in all my classes. When I got to college, the first semester, I was in a section of fifteen girls who took all their courses together. And they were not up to the standard of my high school classmates. They were really far below in spite of the high standards, presumably, for entrance. I should mention that of those fifteen or so girls, only two graduated.

GORTLER: Oh, my. What an enormous dropout rate.

COHN: I think I was put in a very stupid section. I don't know why, perhaps because I was so young. I should tell you one amusing thing about my high school career. In those days, unlike today, there was no counseling or advice given. I went to a high school with five thousand students.

GORTLER: What high school did you go to?

COHN: Evander Childs. Nobody paid any attention to you. So I was quite surprised when in my last semester, I received a note from the dean. I should tell you that I graduated fifth in my class. I guess the class was about five hundred, because we had a graduation each semester. Anyhow, I got a note from the dean saying I should come and see her, which I did. And she said, "You can't graduate." I said, "Why not?" She said, "You're too young! You're too young to get working papers." At that time, even though this was a middle class neighborhood, by far the majority of the girls never went to college. I told her that I didn't intend working and that I intended going to college. She said, "No college will admit you at this age." By this time I was getting a little bit annoyed because there was nothing constructive about what she was telling me. I said, "Well, I've taken all the courses, and I don't see why I can't graduate." I added, "As far as going to college is concerned, I'll take care of that."

GORTLER: You were pretty gutsy even at that time.

COHN: Oh, I sure was. Here was this woman who had never paid any attention to me. Today if they had a fourteen-year-old who was near the top of the class, they would give her counseling, they would tell her she could get scholarships and that kind of thing. Nobody told me that. It was just assumed by my family that I'd go to Hunter College. It was free and in the city, so I went to Hunter College. They didn't question my age at all when I went there. But I have often suspected that perhaps they put me in that group because I was so young. I really don't know. But in any case, that was only the first semester. After that I had different students in every class, because then I could choose my subjects. The first semester you couldn't choose anything. So, in the second semester, I chose to take chemistry. I was really rather disappointed at the level of their teaching in chemistry. I had a woman teacher who obviously had been doing it for years and really didn't know too much chemistry. Nevertheless, I continued the course because I decided that I was interested in chemistry. I then went on and took organic chemistry. I also studied physics. You couldn't major in physics at Hunter at that time. There was no such thing or I might have been a physics major.

GORTLER: Were most of the instructors women?

COHN: Only in the first year. I had two women teachers, one for each semester of general chemistry. After that all my chemistry professors were men. I had a professor of organic chemistry by the name of Friedberg, who was a German. He was an American citizen, but he originally came from Germany. And I really got a sense of continuity in science from him. This man was seventy-five years old when I was studying organic chemistry with him. He had been retired ten years earlier from City College, and he sprinkled all his lectures with anecdotes. When he was twenty-one years old he had been a assistant to [Robert W.] Bunsen. He personally knew [Justus von] Liebig and [Friedrich] Wöhler and he used to tell us tales about them. But we really didn't learn very much organic chemistry, because he was very much behind the times. I remember in the laboratory, he had a test tube of benzene in his hand and he would shake it and he'd say, "These modern chemists who can hear the little hexagons rolling around!"

That was the second course I took in chemistry. He had an interesting way of examining us. At the end of the semester he would hand out twenty questions, and he told us that, of the twenty questions, ten would appear on the final examination. He said that if we knew the answers to these twenty questions, we knew organic chemistry. So it didn't matter that he told us beforehand what the questions would be. But in addition to that, he gave us an oral examination and he would take three students at a time. I still remember, here we were at the end of a course in organic chemistry, the first question he asked us was, "What is the formula for water?" Of course everyone knew that. Then he said, "How do you know?" And that wasn't so easy. The other two classmates floundered, and I finally answered it to his satisfaction. But it was a very interesting experience to have a professor of that kind. He was of the old school. It was too bad he hadn't kept up in organic chemistry. [laughter]

And then I had a professor qualitative analysis who was a Tammany appointee and knew practically no chemistry whatsoever. I still remember asking him why it was that when you heated a liquid, water in particular, that the density changed. And he said, "Oh, that's because the water evaporates and there's less of it." Well, I didn't bother asking him questions anymore! Then I had quantitative analysis and physical chemistry. And the man who taught quantitative analysis was competent and the man who taught physical chemistry was highly competent. And that's probably the reason why I decided to become a physical chemist.

GORTLER: And who was that?

COHN: His name was Hendel. I think his first name was James. He had gotten his Ph.D. degree at Princeton. He taught well and he knew physical chemistry. However, I really was upset when I went to Columbia. I had an inkling that I had a poor education in chemistry. But what I didn't know was that they hadn't even told me what the field was about. I registered in three courses which all dealt with more or less the same material and I didn't realize it. The catalog descriptions were different. Until the advisor to graduate students looked at my choices and said, "Oh, you don't want to take those three courses. They overlap too much."

GORTLER: This was when you went to take your master's degree at Columbia.

COHN: Yes. When I went to Columbia to take my master's degree.

GORTLER: Let's back off just a little bit and go back to Hunter. What other courses were you taking at the time?

COHN: I took all the physics courses they offered, which were very meager. I took semester courses in electricity and in optics. And I took a semester course in mechanics where calculus was not required. You can imagine the level of a mechanics course without calculus! The one good course I did take in physics was the last one I took at Hunter, an introduction to modern physics. That was given by Dr. [Claire] Messenger who was the head of the department.

In my junior year I went to the Sixty-eighth Street campus. I don't know whether you realize this, but at that time, the building at Sixty-eighth Street was not large enough to house all the Hunter students. You didn't get there until you were a junior.

GORTLER: I see. So they had another campus?

COHN: They had several. The first semester was on Eighty-sixth Street where they had only lower freshmen. It was in some kind of Jewish school that wasn't used by the owners except after regular school hours. The space was limited, and I suppose that's the reason they had to have the arrangement that you attend all classes with the same fifteen to twenty students that were assigned to your group. There were also a limited number of courses, and all the courses were prescribed. The next year and a half I spent in a commercial building at Thirty-second Street near Third Avenue. And I was taking organic chemistry which was given at Sixty-eighth Street. They gave us fifteen minutes to get from Thirty-second Street near Third Avenue to Sixty-eighth Street and Lexington Avenue. So you ran all the way to the subway station and hoped that a train would come quickly. Of course, after class you had to go back to Thirty-second Street again. The pace was hectic. But when I got to my junior year I took all my courses at Sixty-eighth Street

Hunter also had a branch in Brooklyn. This was the old Brooklyn College. The women students who were there for two years also came to Sixty-eighth Street as juniors. Many students had dropped by the wayside by this time. I became very friendly with a number of my classmates. But there were very few who were science majors. Most of them were social scientists.

GORTLER: Are there some that you've maintained friendships with?

COHN: Well, one of them with whom I was very close died, but it was quite some time ago. I did form some friendships there certainly which lasted for a while but with their moving from New York and my leaving New York, the contacts lapsed.

GORTLER: Yes.

COHN: Most of them were social scientists. A few of them were in the humanities, but none of them were science majors. We were very serious. We formed something called the Epistemological Society of Hunter College. I pointed out to them that they expected me to know all about literature and social sciences but that they knew nothing about science. They took this very seriously, and they said why didn't I do something about it? So I went to Dr. Messenger, the head of the department who taught a course called The Introduction to Modern Physics for physics minors and said, "Look, I have all these friends who would really like to know something about physics. Why don't you teach the course in introduction to modern physics on a level for non-science majors?" And she did. All my friends took it. It was a very successful course apparently. I anticipated C. P. Snow with his "two cultures" by quite a few years.

GORTLER: So you did in fact take courses outside of the sciences.

COHN: Oh, sure. You had to take a good many required courses. And I took some electives too. You had to take, I think, two years of English, a year of writing, and either a semester or a year in literature. Then I took a course in debating which was an elective course. I took an elective course in philosophy, ethics. Logic was required. I also took a course in history of art, one in acting, and one in physical anthropology. I took an elective in calculus. That's as far as I got in math. Calculus was not required of a chemistry major nor of a physics minor. I'd had two years of Latin in high school. I studied German in college and I went beyond the required courses too. I took a reading course in German which I enjoyed very much. So I took all sorts of courses besides science courses. You see, they didn't offer that many science courses. I took every chemistry course and every physics course that was offered. I should tell you that the chairman of the department of chemistry was a

Southern gentleman who didn't think it was ladylike to be a chemist. He told us that.

GORTLER: Who was the chairman?

COHN: Moore--I am not sure of his first name--I think it was Charles. I remember a contact I had with him after I left Hunter and was at Columbia. After I'd been there for a year, I thought I'd apply for a scholarship and see if I could stay in school instead of having to go and work. So I went to him to ask for a letter of recommendation. You know, I graduated Phi Beta Kappa and was one of the top students in chemistry and so on. I remember walking into his office on this occasion and seeing the JACS [Journal of the American Chemical Society] piled high, with the wrappers still on them, gathering dust. And then I told him what I wanted of him, and he said, "If you persist on this misguided path and continue to do graduate work, I predict that in five or ten years you will be coming to me for other kinds of advice." I felt like telling him that I hadn't come to him for advice but that I had come to ask him to write a letter for me. In view of the fact that I wanted him to write a letter, I didn't say it. And he said, "The advice you will be asking me is, you will tell me that you have met a man of fifty-five who is a widower with five children and should you marry him." Well, this was a little too much for me! [laughter] So I said, "What makes you think he'll have five children? I don't know what kind of letter he wrote for me. I didn't get the scholarship. [laughter]

GORTLER: Before we go on to Columbia, tell me what at that particular point was your conception of being a chemist? Did you have any idea what you were going to get yourself into?

COHN: Not really. You see, I had the vague idea that if I got a Ph.D., I could do research. I really didn't know whether it would be in industry or academia or in a government laboratory. I was really very ignorant; I was not even aware that I would be barred from most positions because of my sex and ethnic background. For example, I had applied to Princeton for graduate work (much to the amusement of Professor Hendel when I subsequently told him about it). I received a polite letter of refusal informing me that only men were admitted to graduate school.

GORTLER: I think most people at that stage are ignorant. I just wonder what they think that they're going to be doing in the future. Had you done any research at Hunter?

COHN: No! There wasn't anyone who did research there. Hunter at that time was very different from what it is today. Ninety percent of the students were education majors. There were many girls who studied chemistry and took as many courses as I did. But they were intending to be chemistry teachers in high school. That was their aim, and that the head of the department approved of, by the way. That was quite acceptable. There was one other girl besides myself who did go on to graduate school. She went to Syracuse, I remember. I wasn't particularly friendly with her, so I don't know what ever happened to her. Most of the students were quite poor and they had to go to work after college. It wasn't as though they had any choice. Also it was the depth of the Depression; I graduated from college in 1931 and it was very difficult to get a job and a very difficult period to be financially able to go to graduate school.

[END OF TAPE, SIDE 1]

GORTLER: You were saying it was difficult to find a job, let alone go to graduate school.

COHN: Yes. And many of the students who were trained in chemistry never did chemistry because they couldn't get jobs. The teaching profession had almost dried up and they were hiring practically no teachers in the New York City public school system. Most of the graduates in those years became social workers. They became investigators for the welfare system because there was a demand and no students were trained for that particularly, so they would take any college graduate. But in any case, I was the only one of my graduating class that went to graduate school at Columbia in chemistry.

GORTLER: Did you think of going anywhere else?

COHN: Oh, I couldn't afford to without a scholarship. I had applied to a number of universities without success. The reason I could go to Columbia is that I had worked summers and I had enough money for the tuition which was at that time $300 a year. I could live at home, so that room and board cost me nothing.

GORTLER: Was there anything particularly interesting about the jobs you had during the summers? Did you work as a chemist?

COHN: No, not as a chemist. I was a counselor in a day camp. I also worked as a salesgirl in Macy's which was another thing that college graduates did in those days. I worked at Macy's on Saturdays during the academic year for quite a while, in the electrical goods department for the last two years that I worked there. I worked there full-time for a month before the day camp started. I preferred the day camp job so I quit. But before I quit the buyer offered me a job as assistant buyer. He offered me a career in merchandising and I told him I wasn't interested. Even though jobs were hard to come by, I wasn't going to become a buyer in a department store. I went to graduate school.

GORTLER: So you got up there and you opted for the wrong courses initially.

COHN: Well, that was corrected and I took a course in organic chemistry, a course in thermodynamics, and a course in the phase rule. J. J. Beaver taught that.

GORTLER: Who taught the organic course?

COHN: It was a lab course and it was officially taught by [Marston] Bogert, but I never saw him. It was taught by his assistant, whose name I don't remember.

GORTLER: And the thermodynamics course?

COHN: One half was taught by [Harold C.] Urey and the other half was taught by [Louis P.] Hammett. It was a year course. What else did I take? Oh, I took a course in physics. I took mechanics. [George B.] Pegram, the chairman of the physics department, taught that. That was a year course also. And then I took a semester course in the history of organic chemistry which [John M.] Nelson taught.

GORTLER: Oh, interesting.

COHN: It was a delightful course. Absolutely the most enjoyable course I took that first year. I also took a course in molecular spectroscopy that was taught by Urey. I took that course without knowing quantum mechanics. I was always taking courses for which I didn't have the background. I got an A in the course too. That's the course from which I had a beautiful notebook which I have contributed to the Urey archives. You had to draw energy diagrams and transitions between energy levels, Hund's Case A and Hund's Case B, and so on. Anyhow, I enjoyed that course very much. I had already decided that Urey was the man under whom I wanted to do my thesis if I should go on with my graduate work.

GORTLER: As a result of being in contact with him as a student?

COHN: That's right. It was the course he gave in thermodynamics. Oh, he often got mixed up and he wasn't the best teacher in the world, but he had such enthusiasm. Occasionally I saw a glimpse of really profound thinking. On the other hand, Hammett was so boring and so soporific. It was hard to keep awake in his classes.

GORTLER: I was going to ask you about that. I'd heard the same thing from a number of other people.

COHN: He was a terrible lecturer. The other thing about Columbia which disappointed me greatly, was the lack of research opportunities. The reason that I went to graduate school was that I wanted to do research. Well, at that time at Columbia (I don't know if they've changed this), no graduate student could do any research until he or she had passed the qualifying exams and chosen a professor to work with and been accepted. You couldn't do that in your first year. And so you never got into a lab unless you took a lab course. I took a lab course in physical chemistry with Beaver which was an excellent course and, as I have already mentioned, Bogert's lab course in organic synthesis. Yes, that was in my first year.

GORTLER: That's a lot of courses.

COHN: Well, some of them were only semester courses. I took thirty credits altogether. And if your grades were good enough, you got a master's degree without a thesis, without an examination.

GORTLER: After a year?

COHN: After a year, and thirty credits. If your grades weren't good enough, you could still get a master's if you took an examination and passed it satisfactorily. I didn't have to take the exam; I was just handed this master's degree after a year of course work. I don't know why they did it.

GORTLER: It may have tied into the high school system. The teachers had to get master's degrees, and they would come back and get masters's degrees with thirty credits of work.

COHN: Maybe so. They had about two hundred graduate students in the 1930s, of whom seventy-five were candidates for a Ph.D. Others were master's candidates and some just took a course or two. Also there were a lot of people who worked and came to take a course or two. In any case, I took the thirty credits that year and I got a master's degree. But I was very disappointed about not being allowed to have the opportunity to do research. One day, I was in the physics department and I saw a notice on the bulletin board which read, "All graduate students interested in doing research should talk to Professor Rabi." Well, I decided this was for me. So I went to speak to [Isidor] Rabi and he said, "Well, you know, if you do the research for me you sometimes have to stay here until midnight,"--that sounded great to me! That was my idea of the real McCoy, you know. That's the way you did research. So everything was going well. Then he asked me what I was doing at the time. I said, "I'm taking a master's degree in the chemistry department." He said, "If you want to work for me, you'd have to switch over to physics." Then I told him that I was going to leave at the end of the year. And he said, "Oh?" He wouldn't take me. "In six months you'd break more than you'd make." He said, "What are you going to do?" I said, "I have to go out and find a job. I have no money. I can't continue as a graduate student." He said, "What kind of job do you think you can get? You know the best you can do is be a saleswoman at Macy's." So I thanked him very kindly but I said that I didn't have the money and therefore I could not stay on.

GORTLER: There was no support for graduate school students at that time?

COHN: There was support for graduate students. There were teaching assistantships. But they were not available to women students because the assistantships were all in Columbia College and Columbia College was an all-male school. They told me that they had had bad experiences with women in World War I--that was even before my time [laughter]--and they would not have a woman as a teacher in anything but graduate courses. Of course, as a first-year student I couldn't be a teaching assistant of a graduate course. There were very few of those.

GORTLER: There were a number of women students at Columbia.

COHN: Oh, yes.

GORTLER: There were so many people who worked for [Henry C.] Sherman.

COHN: That's right. There were a few women students other than Sherman's students.

GORTLER: And how were they supported?

COHN: I don't know whether Sherman had some support for his students or not. That I can't tell you. The ones who were going for master's degrees supported themselves. There was no support for them. There were some scholarships. But you know, they were the kind of scholarship where you had to have been born in some town in Ohio and have parents who were missionaries in China.

GORTLER: So you decided you had to find a job. How did you find a job?

COHN: Well, when I was a senior at college, I took a civil service examination for junior chemists. It's really amusing. It was halfway through my senior year, and I took it as an analytical chemist. I'd only had half of the course in quantitative analysis, so I just read the rest of the book and I passed the exam. Toward the end of the academic year at Columbia, early May, I got a letter offering me a job.

GORTLER: How timely.

COHN: Yes, at the National Advisory Committee for Aeronautics, NACA, which was the predecessor of NASA. I accepted with alacrity. Then came the second telegram, "This job has nothing to do with chemistry. It involves doing computations in aerodynamic research. It is not a junior chemist position; it is a junior scientific aide position." "Well," I thought, "I have nothing to lose. I'll go down there."

GORTLER: This was in Washington.

COHN: No, it was in Langley Field, Virginia. "I'll go down there for the summer and work, and if I don't like it I'll quit at the end of the summer and try to do something else." So I took that job at the end of the academic year. When I got down there, I found out that a junior scientific aide doing computational work meant working what they called a calculating machine. It was a Marchand. I don't know if you know what they were like in those days. They were not even electrical. This was Mark I. If you had to multiply let's say a five-digit number by 333, you banged three times, and then you moved your hand over to the next column and did it three times again and once again.

It was nothing but an adding machine. To do division, you used a table of reciprocals set up in front of you, and you went through the same procedure. Occasionally we did things with a slide rule and occasionally we had to make graphs. But most of it was working this Marchand calculator. There were about six young women who were doing this. They were all college graduates. Another young woman and I arrived at the same time. The ones who were there before us were very competitive. They used to vie with each other to see how many calculations they could do in a day. It was more strenuous than typing away at a typewriter for eight hours a day. In those days, one worked eight hours a day. I decided if I had to do this, I wasn't going to stay. I let it be known far and wide that I was a chemist, and I asked if there was a place in the research establishment there that needed a chemist. Fortunately, someone wanted a chemist. So I went to work in the engine laboratory as a chemist, in the section called Fuel Injection. I worked for the next two and a quarter years on combustion in engines. If you looked at my bibliography, you'd see that the first two papers were on that subject.

GORTLER: "Some Factors Affecting Combustion in an Internal Combustion Engine" (1) and "Combustion in a Bomb with a Fuel Injection System" (2). Research on fuel injection systems was really looking into the future.

COHN: Well, I <u>was</u> in a section called the Fuel Injection Section. This was long before the days of jet engines, you understand. I went down there in May of 1932. At that time they were trying to develop an airplane engine that used the diesel cycle and fuel injection, but with spark ignition. You see an ordinary diesel is much too heavy for an airplane. In an airplane the important thing is the power/weight ratio. They wanted to take advantage of the diesel cycle which is much more efficient than the Otto cycle, but they didn't want to attain such high pressures as in a diesel engine because they didn't want to use the heavy materials necessary to withstand the very high pressure. This research was an attempt to combine the best of both engine types and use spark ignition instead of compression ignition and try out various fuels and so on. I was the only woman amongst seventy men researchers.

GORTLER: My!

COHN: Oh, it was a big institution. They did not only engine research, but aerodynamic research. That was their main thrust. They had a full-scale wind tunnel.

GORTLER: This was your first exposure to real research.

COHN: Not only to real research, but to a job and doing applied chemistry. I don't think I would have gotten very far if I hadn't had a very sympathetic superior. He was really a very smart man as well as a very decent human being. He and I decided to study the physics of statistical mechanics together, for example. He was a physicist; he wasn't an engineer.

GORTLER: What was his name?

COHN: [A. M.] Rothrock. Many years after I left I came across a publication from the NACA. The engine lab had moved out to Cleveland and I saw that he was the director.

GORTLER: So then you decided to go back to graduate school or the job ended?

COHN: I should tell you several things about the job. For one thing, they had given me the rank of junior scientific aide, which was a subprofessional rating, unlike a junior chemist, which is the first rung of the ladder of professional ratings. I didn't realize the significance of that when I accepted the job. I would have taken it anyhow, had I known; I had no choice. I found that to shift from a subprofessional rating to a professional rating was an almost impossible hurdle. The reason was that they didn't want a woman with a professional rating. They told me so. The man who was the head of this whole organization was in Washington. By the way, this laboratory was an independent agency; it wasn't under any of the federal government departments. The man who was the head of it, a man by the name of [George W.] Lewis, was very much opposed to women scientists in the laboratory. He came through the laboratory once, unbeknownst to me. I was working there and I was wearing one of the mechanic's coats, because it was an engine laboratory, and it was not that clean; it was fairly greasy. Anyhow, he saw me and he sent down a directive that I was not to work in the laboratory. So I said, in my usual way, "Well, if I'm given someone to do the laboratory work, I'll sit in here and think up the experiments and have someone do the laboratory work for me!" And indeed that's what happened. They assigned a junior physicist who was in my section. He had a professional rating, and he worked under me. The second paper was by me and Robert Spencer (2). That was the young man who was working for me. How they ever got that past the head of the organization I don't know. But anyhow that's what actually happened. I had designed the equipment and I had done the initial experiments, but after that he did the experiments for me.

In the meantime they were raising my salary. The salary for junior scientific aides in those days was $1440 a year which was considerably less than that of a junior chemist which was $2000 a year. After I was there a month, there was an across-the-board cut of ten percent in all federal salaries. You remember this was the Depression in 1932. So I ended up having a salary of $1300 a year. After two years I was getting $1740 a year which was the top of the scale for a junior scientist aide. I went to see the division chief who was above my section chief and asked him if I had any chance at all of ever getting a professional rating. He said no. I asked him why and he said it was because Dr. Lewis, the head of the organization, didn't believe in having women scientists. I asked him why and he said, first of all they may have men working under them. The fact that I already did hadn't seemed to register. And the other reason was, it would bring on too many divorces. According to him, when a woman professional works with men professionals, the men professionals divorce their wives and marry the professional women. Well, with that enlightened attitude I thought I'd better leave. However, I still needed money. So I didn't leave, but took a leave of absence and went back to Columbia.

I had become very interested in the problem I was working on down at the NACA, particularly the fuel injection. I wanted to be able to study the rate of evaporation of the fuel droplets. It depended, of course, on the design of the fuel injection nozzle and so on. I had gotten the idea that a nice way of studying the evaporation was to do Millikan's oil-drop experiment in reverse which was to charge the particles and keep them suspended in the electric field; as they changed in size they would move, and you would be able to figure out how fast they were evaporating. I thought, "If I'm going back to Columbia, why don't I get a Ph.D. in chemical engineering instead of in chemistry. That's much more suitable for this kind of problem." I was still troubled with lack of money. I thought as a solution that I could take all the course work necessary and then go back and do the research at the NACA laboratory. It was a fine laboratory, with wonderful facilities. The shop facilities were unbelievable. They had an instrument section that designed instruments. You just told them what you wanted and they designed it. Then they had a machine shop that turned out the most elegant work you ever saw. And they had another section of people who put these instruments together. The latter were all former watchmakers. I have never since been in a place where they had facilities like the NACA had in the way of support facilities for the researchers. It was really remarkable. When I came back to Columbia, I found that there were no women students in the chemical engineering department. But I went to see the chairman of the department anyhow. I told him my interests, that I'd been working essentially in chemical engineering and that's why I was considering taking a Ph.D. in chemical engineering.

GORTLER: Who was the chairman of chemical engineering? He was not the chairman of the chemistry department?

COHN: Oh, no. This was a separate department. However, he was in Havemeyer Hall, and the chemical engineering students also were in Havemeyer Hall. In fact, the male students kidded me about it--I had talked to them first. They said I could never take a chemical engineering degree because there was a required power plant course which involved stripping to the waist because it was so hot down in the basement of Havemeyer and I, of course, couldn't do that. I went to see the chairman and I mentioned I had already published two papers. He told me that they hadn't had any women students and they didn't plan to start with me. So that was that.

I went back to the chemistry department and for the first semester I just took courses again because I still didn't have enough course work to take the qualifying exam. Also, I had been away from chemistry for a while, particularly from inorganic chemistry. I had to study it by myself that semester so that I could take the qualifying exam. Let's see, what courses did I take that semester? Well, I took a physics course. I should tell you an amusing anecdote about that. Urey suggested that I should see his friend, Rabi, in the physics department to ask him to recommend what physics course I should take. I went over to see him, and he recognized me. His first comment was, "Much water has flown under the bridges since you were here." I think he'd only been at Columbia a short time when he had put up that notice for students. But by now he'd become well established. In those two years, he'd made a lot of great discoveries and so he was on his way up. He said to me, "What have you been doing these last two years?" So I told him. And he said, "I told you all you could get was a job as a saleswoman in Macy's!" [laughter]

[END OF TAPE, SIDE 2]

COHN: I know I took Urey's course in quantum chemistry and I took two physics courses. I took the physics lab course. It was called the EKA lab--the Ernest Kempton Adams lab. It was a graduate physics lab course. It was a very good course from some points of view. I have one criticism of it which I'll tell you about later. It was taught by a woman, which was unusual. Her name was Lucy Haynor. She was the wife of Bernhard Kurrelmeyer, who was in the physics department at Brooklyn College. She was known by her maiden name, not the name of Kurrelmeyer. She was a very nice person and she was interested in spectroscopy. It had all sorts of really informative experiments in spectroscopy and vacuum tubes. We also did the Millikan oil-drop experiment, and the Zeeman effect. But she set up all the apparatus and we were not allowed to touch the equipment except when we fooled around with vacuum tubes. When it came to using the Hilger spectrophotometer we weren't allowed to touch it, that is, adjust it in any way. And similarly with the infrared spectrometer. I can understand her not wanting us to mess up the instruments but, on the other hand, I don't think that's the best way to teach students how to do experiments.

I also took a course in electromagnetic theory in the physics department that was taught by [Shirley Leon] Quimby. In addition to being a professor of physics, he was a master magician. So he'd look at an equation and say, "Now you do a three-card trick on it...." In addition, I took a graduate course in mathematics on Function Theory of Complex Variables. At the end of that semester, I took the qualifying examinations. To this day, I'm sure that I flunked organic, but they passed me anyhow.

GORTLER: At what point did you run into Mary Caldwell?

COHN: Oh, yes. When I came back to Columbia and decided to enroll as a Ph.D. candidate in the chemistry department, she was the advisor to the graduate students. And so I went to see her. I should tell you their way of grading--some professors gave A, B, C, but some gave pass or fail. In some courses I really didn't know my grade. I had assumed that my grades in the first year were all right because of the fact that they had given me a master's degree without demanding an examination. At any rate, she looked at my record and, apparently, for those pass and fail grades she actually had a numerical grade. Although she never told me what the grades were, she said, looking at my record, she didn't really think it was advisable for me to be a Ph.D. candidate. I was appalled. Since she was leaving it to my discretion whether I wanted to do it or not, I said that I thought I would. After all I was paying my own way and so they had no objections to my continuing, but that was her advice to me. I think I mentioned that many years later, in talking to someone I knew who had come to Columbia as a graduate student ten years later, I learned that Dr. Caldwell said the exact same thing to her. Dr. Caldwell was the only woman on the faculty of the chemistry department. She of course worked in Sherman's domain, as a food chemist in nutrition.

GORTLER: Was Sherman still chairman at that time?

COHN: Yes, I think so. I'm pretty sure he was chairman. I can't remember who was chairman when I first got there, but he wasn't chairman in 1931-1932. Wasn't there a man called Morgan, a physical chemist, as chairman?

GORTLER: I don't know. I don't think so.

COHN: I'm not sure, but I know that when I came back Sherman was chairman. And the scuttlebutt among the students was that they couldn't agree on anyone of the stars in the department, so they chose Sherman as being unobjectionable.

GORTLER: That may have been true. Although I think he'd been chairman for some time.

COHN: Had he?

GORTLER: Yes. Although there may have been some interim period in which he wasn't chairman.

COHN: I'm not sure. I just don't know. Well, in your first year of graduate school, you're not very aware of these things anyhow.

GORTLER: What about choosing a research director?

COHN: I had long since decided that I wanted to work with Urey and then he was awarded the Nobel Prize that year [1934]. So I went to see him--I don't know whether it was just before I took my qualifying exams or after--and told him that I wanted to do my graduate thesis with him. And he said, "But you don't want to be my graduate student. I don't pay any attention to my graduate students." I replied, "That's all right. I still want to be your graduate student." It was true, by the way, that he paid little attention to his graduate students, but he had warned me. I had always been interested in physical chemistry anyhow. I had taken several physics courses and I had taken, I guess, most of the physical chemistry courses that they offered.

GORTLER: Did you have some math beyond the calculus?

COHN: Oh, yes. As I mentioned I had taken a course, Function Theory of Complex Variables, in the mathematics department. I sort of learned differential equations without a course. Don't ask me how. But I did take that Function Theory of Complex Variables, which was a useful course if you were going on in physics and physical chemistry.

I met my future husband [Henry Primakoff] when he was a student in the EKA lab course that Professor Lucy Haynor taught. He was, of course, a fantastic student. He got straight A's in everything--physics and math and all other courses. He was an undergraduate, but he was taking a graduate course in his senior year. They gave him a master's degree at the same time that they gave him a bachelor's degree because he'd taken so many of the graduate courses. He studied as much mathematics as he did physics.

GORTLER: I was just looking at his entry in <u>American Men and Women of Science</u> and I noticed he took a master's degree at Columbia and then he went to Princeton, but then he took his Ph.D. at NYU?

COHN: Yes. He first went to Princeton. In those days, getting into Princeton was equivalent to getting a scholarship. They had very few graduate students. The total number of graduate students in all fields was limited to whatever the graduate college could accommodate. I've forgotten whether it was one hundred or two hundred. This included everything from physics to archaeology. And the tuition was only $100 per year, so it was equivalent to getting a scholarship. Henry had enough money for one year at Princeton. He tried to get a fellowship the second year and he didn't succeed. They gave only one in theoretical physics, the area of physics he wanted to work in. He was the least vain of men that I've ever known, but in later years he said that they made a mistake. They gave it to someone who really didn't ever do anything in theoretical physics. He had to get a fellowship somewhere if he was to continue his studies. He couldn't stay at Princeton; he couldn't afford it. One of his professors was Ed [Edward U.] Condon, and Ed Condon thought very well of him. He was a friend of Dr. [Allan C. G.] Mitchell, the man who was head of physics at uptown NYU. Mitchell later left NYU and became head of the department at Indiana. Ed Condon wrote him a letter saying, "Look, we have a very good graduate student and he needs a fellowship. I recommend him highly to you." So they gave Henry a fellowship and that's why he went to NYU.

I stayed at Columbia and, again, had no financial support. The teaching assistants at that time were paid $700 a year. There were one or two exceptions, people who worked twice as many hours as the others, and they got twice as much money. But there were only one or two of them in the department. There was one university fellowship and that went to T. Ivan Taylor, a fellow graduate student in Urey's lab.

GORTLER: "Toughy" Taylor.

COHN: Yes, and for good reason. He had already shown his ability to do research. He had two papers published in JACS before he ever came to Columbia. He was a very good experimentalist, really very good, but he wasn't a particularly fast thinker. Now, Urey on the other hand had a very fast mind. I've worked with many of the greats. Almost everyone I've ever worked with was a Nobel laureate, but of them all, Urey had the fastest mind. It was amazing. Once a week, he expected me to tell him what I was doing. And I used to have to prepare myself very carefully because I'd start on number one and number two and he was down to number five already by the time I got through telling him about two. So I would think the things through very carefully. When he and Toughy used to have a conversation, it was like two monologues. They weren't on the same wavelength. But anyhow, Toughy was a wonderful experimentalist.

The first thing Urey had me do were theoretical calculations. My problem was to be the separation of ^{12}C from ^{13}C. At that time Urey was busy separating isotopes. He also had some other graduate students who were doing spectroscopy, for example, Raman spectra of methane and deuterated methanes. There was one student doing all the species between CH_4 and CD_4--CD_3H and so on. But he wanted me to separate the carbon isotopes. He was using chemical equilibria of isotopic reactions to separate isotopes where the equilibrium constants would vary slightly from one. If you have multiple plates, that is multiple equilibria, that's how you enriched one isotope. It was done always in a two-phase reaction so that you would enrich in one phase and deplete in the other phase. He had me do theoretical calculations, starting with spectroscopic data and getting equilibrium constants from partition functions. Even though you didn't know the total partition function, you could always calculate the ratio of the partition functions of the two isotopic molecules. The calculations were also done as a function of temperature so you knew not only which reaction would give you the best fractionation factor but at what temperature that would occur. After three months of such calculations I came up with the fact that if you could bring carbon monoxide and carbon dioxide to equilibrium, you could get the highest fractionation factor for ^{12}C and ^{13}C of any of the reactions that he'd told me to examine. I should tell you, that was my second semester in his lab. The first semester he had me learn how to blow glass and I had to repeat an experiment that one of his postdocs had done.

GORTLER: I was going to ask you about that because I know in a couple of publications you showed a vacuum line and you said a tube had to be sealed onto the vac line. I was wondering who had done that. I take it you did that. Tell me about learning how to blow glass.

COHN: Urey said that although we had a glass blower at Columbia, one might in the future be in a place without one and so he thought everyone should know how to blow glass. He had a postdoc whose name was Wald. He came from Illinois and he was a marvelous glass blower. That fellow taught me how to blow glass. It was a very useful thing to learn because, you see, we worked mostly in vacuum systems. We had to set the experiments up ourselves on the vac line.

The first problem that Urey assigned me was the repetition of a postdoc's experiment on the isotopic equilibrium of $H_2{}^{18}O$ and $C^{16}O_2$. The sample of water available was isotopically enriched in both ^2H and ^{18}O and the deuterium had to be removed from the water before its ^{18}O content could be determined. The separation of the ^2H and ^{18}O in the sample was done electrolytically. The recombination of oxygen with isotopically normal hydrogen was done by burning normal hydrogen in a stream of enriched oxygen in a closed system. The enriched form of water in half of the electrolytic cells supplied the oxygen and ordinary water in the other half supplied normal hydrogen. In any case, it was just practice for me to learn vacuum technique and in general how to do experiments. The answer had already been obtained by a postdoc. The question was, would I get the same answer? Eventually I did.

I also had to learn how to analyze for deuterium content of water; in those early days it was done by measuring density of the water with a Cartesian diver in a closed system where the pressure on the water could be controlled. The sample tube was kept in an ice-water bath, so that the temperature was constant, and the diver was observed through the cross hairs of an eyepiece. You then changed the pressure which changed the density of the water and the float would either rise or fall depending on whether the density of the water was greater or less than that of the diver. By determining the pressure that was needed to get the diver to float, you knew what the density was, therefore you knew the deuterium content. That method was good to a half part per million in density.

GORTLER: That's extremely accurate. The method seems very crude.

COHN: It wasn't crude at all because the pressure doesn't change the density that much. So you get a big change in pressure for a rather small change in density.

GORTLER: Yes.

COHN: But the real difficulty with the method is to have the water pure enough. So we had to devise ways of purifying the water.

GORTLER: You must have had very, very small amounts of water.

COHN: No.

GORTLER: Was the water generated through some conversion?

COHN: Yes. When I got to biochemistry, we had to use small amounts. But in chemistry, using these divers, you needed several milliliters of water to do the analysis. Later we used methods where we needed only microliters.

In my first semester in Urey's research lab, I learned how to blow glass, I repeated a postdoc's work and I learned how to do deuterium analysis. Then I went back to my job at the NACA for the summer to earn money. That was the summer of 1935. I had come back to Columbia in September of 1934. It so happens that during the year 1934-1935, there was a meeting at Columbia of the Aeronautics Association. I thought maybe some of the people I knew at the NACA might be at the meeting. So I wandered over and who should I see but the head of this whole organization who had...

GORTLER: ...booted you out of the laboratory.

COHN: That's right. He greeted me very graciously and he said, "Miss Cohn, you're a very personable young woman. Why don't you get yourself a job teaching, at Bryn Mawr College, for example?" So I thanked him and I said I really wasn't interested in teaching, that I was interested in doing research. But his notion that I could get a job at Bryn Mawr College was naive. [laughter] Of course, he was trying his best to get me out. I was still on leave of absence; I hadn't resigned yet. I went back for the summer. I couldn't take another leave of absence, so I quit.

I came back to Columbia and I started working on the $^{12}C/^{13}C$ separation problem. I'm not sure just when I did the calculations--whether it was before that summer or not--but it was before I started the experiments. The experiments, of course, depended on analyses on a mass spectrometer. You couldn't use density methods for carbon isotopes. I tried various ways of making the two gases CO and CO_2 come to equilibrium. But the mass spectrometer wasn't working, so I worked the whole year in the dark without knowing the results of a single experiment I did. And finally when June came around and the spectrometer still wasn't working, Urey said, "Well, this won't do. You go down to Princeton and [Walker] Bleakney will run the samples for you."

GORTLER: Was this the year that Urey was having the machine built?

COHN: Yes. That's right. That was the year that [William Wallace] Lozier was trying to construct a mass spectrometer. He was a student of [Alfred O.] Nier's and then he'd been a postdoc at Bleakney's lab at Princeton. Bleakney was probably the outstanding mass spectroscopist in the country at that time. Urey called Bleakney and asked if he would do the analyses and he agreed, so I went down there will all my flasks of gas. Someone took me in a car.

GORTLER: I was just picturing you getting on the train with all those flasks.

COHN: Oh, no, I went by car. At any rate, it took a day or two to analyze all the samples, and every experiment was negative. At that point I was ready to quit graduate work. But my future husband talked me out of it, and Urey was very apologetic. He said, "I'll never give a student a problem again that depends on an instrument that isn't operational yet." Well, I had wasted nine months.

Urey had just succeeded in enriching ^{18}O and there was a paper published on how to analyze water by the falling drop method. By the way, I wrote an article on that method for <u>Preparation and Measurement of Isotopic Tracers</u> (3). The method in its original form had been published by the physiologists [A.] Krogh and [H. H.] Ussing in Copenhagen (4). They used an automatic pipette and a tube filled with a mixture of two organic compounds that was very close in density to the density of water--the organic compounds were immiscible with water. The principle of the method was based on Stoke's law. The automatic pipette produced a drop of water of constant size into the tube filled with the organic mixture. You had to have the tube in a constant temperature bath slightly higher than room temperature that was constant to a thousandth of a degree. Eventually the drop of water would come to temperature equilibrium and start falling. The tube had rings etched at two places, and you timed the rate of fall of the drop between the marks with a stop watch.

A calibration curve was constructed with salt solutions of known density and the ^{18}O content of the water was determined from the curve. The method was good to one part per million. It took much less water because the drops were small. I don't remember exactly what size they were but they were of the order of 10 microliters. You could do the analysis several times with a tenth of a milliliter of water. From that point of view this method was much better than the Cartesian diver method.

GORTLER: This is for ^{18}O as opposed the D_2O, right?

COHN: No, it could be done with either $H_2{}^{18}O$ of D_2O since the density of water was measured. The objection to this method for determining ^{18}O is that when you purify water for deuterium analysis, you use oxidizing agents. You use alkaline permanganate or chromic trioxide and you don't introduce any hydrogen. But who knows what you're doing with oxygen.

GORTLER: Right.

COHN: You really have to worry about exchange with these oxidizing agents and dilution of your sample. It turned out that someone else in the lab was investigating water oxygen exchange with inorganic anions like permanganate and chromate. They don't exchange that easily, although they do at high temperatures. But anyhow, I had no other analytical method. So Urey suggested a problem that I could do with a method other than mass spectrometry. The first thing I was given to do was to try some organic compounds with different functional groups containing oxygen, and determine which ones exchanged with water at a reasonable rate. Later, when the mass spectrometer became available, I used water that was lighter than normal--that is, with a deficit of ^{18}O--which gives a much bigger analytical range. The normal abundance of ^{18}O is about 0.2%. Urey had only concentrated ^{18}O to about two and a half times normal abundance. At best you had a range of 2.5. But if you went from 0.2% ^{18}O to zero you had a tremendous range. So when I got to use a mass spectrometer, I did practically all my thesis work with water that had been depleted of ^{18}O, because it gave a much bigger range.

[END OF TAPE, SIDE 3]

COHN: I went through a series of compounds. I used ketones, aldehydes, carboxylic acids and hydroxyl compounds. I found that acetic acid exchanged very slowly, but trichloracetic at a rather rapid rate. I later found out that aldehydes exchanged, the rate depending on the particular aldehyde. I found that acetone exchanged at a fairly convenient rate. I reported all this to Urey. He said, "Why don't you investigate the exchange of acetone and water in the vapor state?" So I tried it and I found that acetone and water did exchange slowly at 80°C. The exchange in the liquid state proceeded at a much faster rate even at room temperature. I realized that if I investigated the reaction in solution, I could study acid catalysis and basic catalysis and so on. So I went to Urey and I said, "Yes, it exchanges in the vapor state, but it also exchanges at quite a nice measurable rate in the liquid state at room temperature." I said, "I'd prefer to study this reaction in the liquid state." He shook his head and he said, "I understand what goes on in the gas state, and I understand what goes on in the solid state, but the liquid state is a complete mystery to me." And he added, "I don't like to do experiments where I have no theory to guide me." But I kept at it. I said, "You know it really would be much more interesting to study the exchange in the liquid state because I could investigate acid catalysis and basic catalysis." He said, "Well, if that's what you want to do, why don't you go and speak to Professor Hammett. He knows all about what happens in the liquid state." So I did. I went to Hammett and he was very helpful. He had a fantastic encyclopaedic memory for references. He told me to look up references on the hydration of keto groups and so on. And he would say, "Transactions of the Faraday Society, such and such a volume, such and such a page." It was amazing.

GORTLER: Well, he must have been writing his book at that time (5).

COHN: Probably.

GORTLER: His book was published in 1940.

COHN: Yes. He was working on it. But he really knew all these references. In fact, the results of my thesis problem are in his book.

GORTLER: It's a good classical physical organic problem.

COHN: Yes, it was. I was very proud at the time that my thesis was discussed in Hammett's book. But anyhow, Hammett thought it was a good problem to study and so Urey didn't bother me anymore. He said, "Okay, if you want to do that, go ahead." He was very permissive. He had a very interesting philosophy. He thought that graduate students should be left on their own, but postdocs were there to work on problems that he wanted them to do.

GORTLER: He was paying their way.

COHN: Well, not that. I think he didn't look at it that way. He thought the way to train graduate students was to let them sink or swim.

GORTLER: I see.

COHN: But as far as postdocs were concerned, they had already done their graduate work. They were there to carry out research that he was personally very interested in.

GORTLER: As the problem proceeded, did he offer you advice?

COHN: As the problem proceeded, the mass spectrometer started working. I needed a method for analyzing ^{18}O in water, and it was much better to do it by mass spec than by the falling-drop method. First of all, it would take less material. Secondly, it didn't have the undesirable feature that you might be diluting the oxygen by purifying the water. And so he devised a method for doing that when I had to do it.

GORTLER: Urey did?

COHN: Yes. I was doing acetone-water exchange and he said, "I tell you what you can do. You can take the water and exchange it with CO_2 and measure the ^{18}O in the CO_2. In that way, since we know what the equilibrium constant is for the reaction, you'll know what the concentration was in the water." You have to measure the amount of CO_2 and the amount of water, but still it was very convenient because you could do many samples at one time. And I studied the water-CO_2 reaction as a function of time to find out how long it took to equilibrate water and CO_2 with shaking and so on. It was a two-phase reaction, after all. I also figured out how to separate the CO_2 and water. You didn't want any water in the mass spectrometer; that's deadly for the vacuum. The mass spectrometer was working and I started using water that was lighter than normal, that is, depleted of ^{18}O. The mass spectrometer worked very well for analyzing the CO_2 for its $^{18}O/^{16}O$ ratio. Other than devising the analytical method, Urey really wasn't very interested until I was all finished and I wrote it up.

I wrote my thesis up as a paper for publication (6). At that time at Columbia, in order to get a Ph.D., you had to present the university with 150 printed copies of your thesis, or you didn't get your degree. If you were in science, you had the option of publishing it and using a reprint with a special cover and two special pages, a title page and a C.V. at the end, to meet the requirement of the printed copies. My father was in the printing business, and I asked him how much it would cost to print that thesis. It had eight figures in it. At that time it was very expensive to print figures. He told me it would cost him $1000. In those days that was a lot of money!

So I decided that I would write it up as a paper and then present the reprints. After I wrote the paper, I gave it to Urey to read. I had written "Cohn and Urey" as the authors. So he said to me, "You know, I always wonder why my students put my name on their papers. Do they think I contributed something, or do they think it would give the paper more prestige?" I said, "A little of both." He was satisfied with that. And he left his name as a coauthor. But then he read it and he was so intrigued with the equations I had written and the mechanisms, that he got interested in the work and he started writing kinetic equations and solving them and so on. It was really very interesting that once he saw the results, even though he'd shied away from the liquid state, he got very interested in the analysis phase.

GORTLER: It's a very organic paper, too. It's really a foundation paper in organic chemistry.

COHN: Well, I think I told you it's still being referred to in the <u>Citation Index</u>. It was published in 1938 and so it's had a long life. Though I must say, it may have something to do with the inclusion of a method.

GORTLER: The mechanistic implications were important for the foundations of organic chemistry.

COHN: The rate of enolization of acetone was known from studies of the exchange of hydrogen for deuterium. I showed that this was not the mechanism in this case, that the mechanism must involve the hydration because of the fact that this rate was much faster than the enolization.

I finally finished, but a lot of things happened on the way, needless to say. For one thing, I had no financial support. They had a student aid program where you could earn forty dollars a month if you did work for it. Urey said, "I'm going to get that for you and the work I want you to do is your own thesis." So I got forty dollars a month in my third year, for the academic year.

GORTLER: Now all this is while you're still living at home.

COHN: Oh, yes. But I had run out of money. I had saved enough money on that job, even with the salary I was getting, to pay my tuition. I didn't have to pay room and board, but I had to buy my own clothes, and I had to have money for lunch and incidental expenses. I saved, I think, about a thousand dollars on that salary in the little over two years. And then I worked again the next summer, and I earned some money. What I want to make clear is that Urey was the only member of that faculty who, in my opinion, really cared about the underdog--namely the graduate students. At the end of that year the forty dollars a month I had been getting ceased, as he knew. One day he said to me, "Miss Cohn"--he was always very formal and he always called me Miss Cohn,--"What are you doing for money?" He said, "I know you're not getting the forty dollars a month anymore." I answered, "I'm borrowing it." He said, "You know, ever since I've gotten the Nobel Prize, I've wanted to help my students. Why don't you let me lend you some money and someday when you have a good job, you can pay me back?" So I thanked him, and I said that was very nice of him, but that I was borrowing from my family and I felt more comfortable doing that. But can you imagine a professor today, or for that matter even then, doing something like that?" There weren't many.

GORTLER: Occasionally I'll run across somebody, but you're right, not many.

COHN: He really was concerned. I don't know how much you know about his background, but he came from a very poor background.

GORTLER: Not very much, I just know that he was from the Midwest.

COHN: That's right. And he almost didn't go to high school. He said that the town in which he lived didn't have a high school, and he had to go out of town to go to high school. He couldn't have done it except that an uncle of his died and left him three hundred dollars, so he got to go to high school. He still remembered that, and he really was very caring about graduate students.

GORTLER: So you never did teach as a graduate student.

COHN: Never.

GORTLER: How big was Urey's group?

COHN: He had about three postdocs and about four graduate students.

GORTLER: Did you have interaction with the other students?

COHN: Oh, sure. We were all very friendly.

GORTLER: Who were some of the people in the group at that time?

COHN: Graduate students?

GORTLER: Yes.

COHN: Well, one was T. Ivan Taylor and another one was Alec Mills. He became the director of research of Houdry Process Corporation in Pennsylvania, in Marcus Hook. And Taylor, as I told you, became a professor at Columbia. There was another fellow by the name of Miller. He was doing spectroscopic work. I don't know what happened to him, he was the fourth student.

GORTLER: Who were the people you were closest to? Who did you communicate with?

COHN: You mean scientifically? Well, I was very friendly with all these fellow graduate students.

GORTLER: Okay. Were you friendly with people outside your own group? I don't know who would have been there at the time.

COHN: Oh, yes. I knew a lot of graduate students. You know, not intimately.

GORTLER: I meant people who you discussed chemistry or your work with.

COHN: Sure. I knew Hammett's graduate students. And I had a taste of a very unpleasant experience that sometimes happens in science from one of [Victor K.] LaMer's graduate students. After I set up the falling-drop method, he was working with deuterium and he wanted to use that method. So he came over, and I showed him my set up--which was a replica of Krogh and Ussing's apparatus; it was not original with me. But it was a very accurate method because the pipette was precise. It had been constructed by a very good machinist that Urey had working for him. The only contribution I made was that I found out that the original authors had done the calculation incorrectly. They took the density to be a function to the time of fall when actually it's the rate of fall, and I pointed out to him that that was an error, and that they should have used the reciprocal of the time, not the time. Well, he went and set up a system that was ten times less sensitive, because he had a crude home-made pipette in which he greased the piston and it wasn't an automatic pipette. In any case, it was ten times less accurate than the one I had set up. And he published it and pointed out that Krogh and Ussing had made a mistake in their calculations. You know, when I saw that I was so horrified that he would do this to me that I went to Urey and said, "Look at this student of LaMer's, he published what I had told him. And the only new thing in his method is this correction of the calculation." Urey said, "Calm down, calm down. This is the first time it's happened to you. It won't be the last!" [laughter] He was fairly cynical. He assured me it had happened to him too.

But I knew several of Hammett's graduate students because their interests were really closer to mine.

GORTLER: Who was there?

COHN: There was a fellow by the name of Roberts.

GORTLER: Irving Roberts?

COHN: Right. Do you know him?

GORTLER: I don't know him, but there's a very famous paper by Roberts and Kimball that everybody thinks is written by Jack Roberts but is written by Irving Roberts. It's on the bromonium ion (7).

COHN: Oh, really?

GORTLER: Yes.

COHN: Oh, I'll tell you an interesting thing about Roberts. When I finished, Urey couldn't find me a job. He and I both went to an ACS meeting and when he came back, as I told you before, he said, really very sadly, "Nobody wants you." And so he offered me a postdoctoral position. He asked me what kind of problems I wanted to work on. I had gone and read a book on organic reactions, and I found ten reactions that you could study with ^{18}O. You know, there were so many. It was an untouched field. So I started telling him about these ten reactions, mechanisms where at least the point of bond cleavage could be determined. And he said, "You know, you're the first graduate student I've had who had some ideas after they've finished their thesis." I said, "Yes. Graduate student training does tend to lead to sterility, doesn't it." [laughter] Anyhow, he offered me a job as a postdoc, and I was pleased to take advantage of it. I had an open field with no competition since he was the only one that had any ^{18}O. It was a golden opportunity to do a lot of these reactions, and so I accepted. A few weeks later, [David] Rittenberg and [Rudolf] Schoenheimer from Columbia's medical school got in touch with me and told me they had a job for me with [Vincent] du Vigneaud in biochemistry using deuterium as a tracer. This wasn't my first contact with Rittenberg and Schoenheimer. They used to come down to Columbia quite frequently because they used to get their isotopes from Urey and also to talk to him.

GORTLER: Rittenberg had worked with Urey?

COHN: Yes. He'd gotten his degree with Urey a couple of years before I did. I had first met him in the 1931-32 period when I was a first year graduate student. When I was working in Urey's lab, he used to come down from P & S [College of Physicians and Surgeons], and he would tell me what he was doing and Schoenheimer would also tell me what he was doing. It all sounded very interesting. Besides, this was a real job. After all, the postdoc position in Urey's lab was offered because I had nothing else. So I went to Urey and we talked about it, and he advised me strongly to take it. He said, "It's much better not to stay in the department in which you got your degree because no one will ever look on you as anything but a graduate student." He also thought this was a very interesting field to get into, so I decided to do it. Irving Roberts had finished his degree about six months before I did, and he had been pounding the pavement looking for a job and he had no job. And I thought he was good. So I said to Urey, "Look, why don't you hire Irv Roberts. He will be very interested in doing the ^{18}O problems, and I'm sure he'll do it well." He was a student of Hammett's. So that's how Irv got to do that work that he did on ^{18}O. He did the mechanism of esterification or something similar.

GORTLER: I don't remember what he did with Urey, but I guess I knew he worked for Urey.

COHN. Yes, he did. And that's how he happened to work for Urey because I suggested to Urey that he hire him instead of me since I had decided to take the other job.

GORTLER: So you had a pretty good rapport with Urey?

COHN: Oh, yes. I had a very good rapport with Urey. I can tell you a lot of stories about me and Urey. He used to tell me all kinds of things.

This was all during the heyday of the Nazis. There was a very political atmosphere. Everyone was aware of it, certainly at the university. Urey had a postdoc who was a Nazi, but Urey didn't know it. In fact, no one knew it except me. He used to tell me. He was a Dutchman, and he used to get the illegal Nazi newspaper from Holland which he showed me. There were a group of German exchange students at Columbia who had been sent over by the Nazi government, and they had some kind of club or group to which he belonged. When the Führer would make a speech, he would tell me that the media in this country were very unfair to Hitler, and they hadn't done justice in translating his speech. Therefore he and his friends were producing the correct translation and passing it around. He was a charming fellow by the way, he really was. And after he left, I happened to mention to one of the professors that he was a Nazi. And he said, "How could he be? He was such a nice fellow."

Anyhow, Urey discovered anti-Semitism. He didn't know about it up to this point. He really didn't. And at one point he said to me, "You know," he said, "Why don't you go out to the Midwest where there's no prejudice and marry a non-Jew and forget that you're a Jew? Then you won't have these problems." So I said, "Has it ever occurred to you that maybe I don't want to forget that I'm a Jew?" He was genuinely surprised that one wouldn't want to get rid of such a handicap. However, he learned a great deal as the years went by and he was later on the board of governors of the Technion in Haifa, Israel.

He was a very good friend of Rabi. In fact, Rabi has related an incident in their relationship in a profile of him in the New Yorker Magazine. Rabi personally told me the story. Urey got money from various foundations for research because he was a Nobel laureate. There weren't many around in those days. He was the third American to be awarded the Nobel prize in chemistry. He was one of the few who had postdocs, you understand. Hammett had Frank Westheimer as a postdoc.

GORTLER: But Hammett didn't support Westheimer. Westheimer had a National Research Fellowship. I don't think it was until after the war that Hammett had enough money to support any postdocs.

COHN: Well, Urey did. He had three or four at any given time. He had money which most of the other professors did not. The university used to support everyone at a low level.

GORTLER: Yes.

COHN: The university grants were not enough to support students or postdocs. But Urey used to get money, even without asking for it sometimes. So one day, he went over to Rabi and he said, "Look, I think the work you're doing is great. I just got $10,000. Why don't you take $5,000 of it to do what you like?" Rabi said that meant the world to him because he wanted to buy a magnet and he could now. That story is in print in the <u>New Yorker</u> profile. Urey was genuinely interested in science and seeing science progress, and he did his best with everyone that he could. He had good judgment, for example, in supporting Rabi. Rabi at that time was a rather junior member of the physics department, he hadn't been there very long when this incident occurred.

GORTLER: Let me ask you a little bit about some of the other people in the department. Victor LaMer was another physical chemist. He got a lot of students but he did have some bad interactions. I just don't know anything about him.

COHN: Well, I don't know what the source of it was, but among the students the scuttlebutt was that he and Urey didn't get along at all. It was rumored that they flunked each other's students in their final orals. You know, students tell such stories. Whether it was true or not, I don't know. I remember the day that it was announced that Urey got the Nobel prize; the story went around that LaMer stayed home sick that day. You know, students develop such myths; the facts may not be accurate but the spirit is right.

GORTLER: I don't think he got along well with Hammett either, but I don't know. I thought maybe you knew more about that than I did. Louis was too much of a gentleman to say anything about it, but he hinted to me that he didn't care too much for LaMer.

COHN: Well, Urey never said anything either. So I don't know it from them. But I think both of them were really so much better scientists than LaMer was. I remember one time when Otto Halpern from NYU was giving a colloquium and he put an equation on the board. LaMer asked what that equation was, and Halpern told him it was the Grunwald-LaMer extension of the Debye-Hückel theory.

With great joy he told him that!

LaMer did very nice work, actually. He had very good students. But he did not have a reputation of being a great mind, and I don't think he was. For example, he stopped me in the hall one day and asked me how my work was going. He knew that I was studying the acetone-water exchange reaction. I said that I had found out that the exchange reaction was general acid catalyzed. And he said, "That's just what I would expect and base catalyzed as well." And a month or two later he met me again and he asked me how things were going. I said that I had investigated base catalysis and I found that it was not general base catalyzed, just hydroxyl ion catalyzed. And he said, "That's just what I would expect." [laughter] That I remember. But personally, I never found him objectionable. I mean I didn't have respect for him. I don't think any of the students did--as they had for Hammett and Urey. But nevertheless, he did nice work, and he had some very good students. He had one very good student by the name of Greenspan.

[END OF TAPE, SIDE 4]

GORTLER: You were telling me about Joe Greenspan.

COHN: What's ever happened to him? He went into business I know.

GORTLER: Yes. He went into business in Brooklyn. He was making instruments.

COHN: Yes. Making instruments. I knew him at that time, but I've lost track of him.

GORTLER: That's all I know about him. I would like to talk to him sometime. I may try to get in touch with him.

COHN: Well, he was admittedly the best student that LaMer had had in a long time. And also the best graduate student in the department when he got his degree. And I don't know who suggested that he should be made a faculty member. It never came to pass, and it was obvious to everyone concerned that the reason was that he was a Jew. I should also tell you that in 1936 when Roosevelt was running against Landon, Urey sported a Roosevelt button. But he was the only member of the chemistry department who did. The others all had Landon buttons.

GORTLER: Another student who was there--Joe Steigman?

COHN: Oh, yes. I knew Joe Steigman. I guess he went to Brooklyn Poly, didn't he?

GORTLER: Right. I've talked with him. I wondered whether you had much interaction with him or not.

COHN: I knew him, but I didn't interact with him much scientifically.

GORTLER: Was George Kimball on the faculty then? He was a physical chemist.

COHN: Kimball came after I left. Just after I left. He was hired I think instead of Greenspan. I'm not sure of that, but it's about the right time.

GORTLER: Okay. And Marston Bogert was there. You took an organic course with him I suspect.

COHN: That was in 1931-32.

GORTLER: Okay. Was he still there?

COHN: I don't know because I didn't have anything to do with the organic chemists after that. [Robert C.] Elderfield was the leading organic chemist, I believe.

GORTLER: He came around the time you were a Ph.D. student.

COHN: That's right. He was on my Ph.D. examining committee. I had a very distinguished committee.

GORTLER: Who were the other members of your committee?

COHN: Well, Hans T. Clark was chairman. He was professor of biochemistry at P & S. He was really an organic chemist. And Hammett was on it and Urey of course. And [Charles O.] Beckmann and Beaver, Elderfield, and [Polykarp] Kusch.

GORTLER: That's a substantial-sized committee too.

COHN: Yes. Seven people. They always had seven people, and two usually outside the department. The two outsiders were Clark from biochemistry and Kusch from physics. Rabi just came, he was not on the committee. Rabi and LaMer came uninvited. When Urey asked me to suggest names, I had deliberately left LaMer's name off the list. But he came and was very pleasant; he didn't make any trouble for me. You see, anyone could come. Rabi came because he was a friend of Urey's and he knew me, too. But he was not an official member of the committee. They both asked questions. That was permitted, theoretically, but I was surprised.

GORTLER: Konrad Bloch must have been around during that period.

COHN: He was at P & S.

GORTLER: Was he working with either Rittenberg or Schoenheimer?

COHN: He was working with Schoenheimer. He was a graduate student at the time.

GORTLER: But you would not have interacted with him.

COHN: Oh, I did for a short time because you see, when I took the job with du Vigneaud, I first spent about two months at P & S in Rittenberg's lab learning the techniques for converting organic compounds to water so they could be measured for deuterium. Konrad Bloch was a student then and so was David Shemin. These were all Schoenheimer's students. Sarah Ratner took her Ph.D. qualifying exams the same time I did and so did DeWitt Stetten. Do you know who he is?

GORTLER: No.

COHN: Well, Sarah was a student of Hans Clark, and Stetten was a student of Schoenheimer. He later became a high administrative official at NIH. Sarah, of course, did very well in her research at the Public Health Institute of New York. Rittenberg died some time ago, about 1970. But those were the people that Schoenheimer had in his lab. They were very good people. Rittenberg, David Shemin and Konrad Bloch became outstanding biochemists. Sarah was a postdoc with Schoenheimer. Everyone of these people has made a name for himself and herself. It was really quite an amazing group of people; all are members of the National Academy of Science and Konrad Bloch is a Nobel laureate.

GORTLER: So at this point you're leaving New York and you're going to go to Washington to George Washington University and work for du Vigneaud. You said initially du Vigneaud did not want you.

COHN: No, because I was a woman. I have talked to other women of my generation, and they tell me that even though their professors took them on as graduate students, they never really expected them to have careers, particularly if they were getting married. Urey never took that view. He assumed that I would have a career whether I was married or not.

GORTLER: You were very fortunate.

COHN: Yes, from that point of view, because I know women who told me that their professors didn't bother trying to get them jobs. Particularly if they were getting married.

GORTLER: Now at that point, when you went to work for du Vigneaud, did you know you were getting married?

COHN: Oh, yes. I knew I was getting married. And Urey had found out that I had, as he put it, "a special friend," but he didn't know whether I was getting married or not. Neither did du Vigneaud. I went to work for him on November 1, and I got married the following May.

GORTLER: But by that time, du Vigneaud was coming to New York.

COHN: Yes. By that time I knew that du Vigneaud was coming to New York. I didn't know that when I went to Washington. I only stayed in Washington that one year, not even a full year, because I didn't actually arrive there until December. So I only spent about eight months in Washington.

GORTLER: How did they convince du Vigneaud to take you?

COHN: They told him that I was the only one in the country that was qualified. There weren't very many people who knew how to handle stable isotopes at that time, or isotopes of any kind, for that matter.

GORTLER: You probably had more experience than anybody, so it wasn't very far from the truth.

COHN: It wasn't far from the truth, and those others who did know how to handle isotopes had better jobs. This was a postdoc position, after all. It wasn't a real job in the sense of a faculty position.

GORTLER: How much were you getting paid with du Vigneaud?

COHN: I was paid well by the standards of those days. I got $2,000 a year. I think the instructors at Columbia were getting $1,800, and assistant professors, I believe, were getting $2,400. So $2,000 was not a bad salary.

Since you wanted to know what Columbia was like in the chemistry department from the students' point of view, it was really quite an unfriendly department. For one thing, the students were almost treated as though they were dispensable. For another thing, you had to pay for every chemical and every expendable item that you used.

GORTLER: I don't think Columbia was unique in that respect. I think I've talked to people who went to graduate school at Harvard and had to do exactly the same kind of thing.

COHN: Really? But it was the attitude of the administration that was really bad. For example, the last summer I was there, I had taken all the courses and credits necessary for a Ph.D. The summer session of the university ran from July 5 to August 10; classes stopped sometime towards the end of May. I could work in the lab until July 5 and work again from August 11 until the fall semester started without registering or paying any fees. But if I wanted to work between July 5 and August 10, I had to register as a student, and I had to pay fees for a course called Research, and I had to put down a deposit for laboratory equipment and a registration fee. All of that came to about eighty dollars. I went to the woman who was the departmental administrator, and I said to her, "Look, this is my last summer here. I'll be finished in the fall, and I have all the credits I need. Do I really have to register for the summer session?" She said, "Why don't you want to register for the summer session?" I said, "Because I haven't got the money." And she said, "I've known students who starved and paid those fees." I was so upset by that that I walked out, and I did not work in the lab those six weeks.

GORTLER: Boy, it was an unfriendly department. What was the story you told me about their sending you a bill after you graduated?

COHN: Oh yes. That was after I left the place. I think I told you that the graduate students got together, and they found out that the storeroom was charging them more for chemicals and equipment than the local supply companies were charging. It was probably to pay for the upkeep of the three people who ran the storeroom and so on. So the graduate students, most of whom had very little money, got together and each member of the graduate student group would take a turn every two weeks and ask you what you needed. You may have needed, for example, glass tubing or a certain chemical, and they went down to Eimer & Amend and bought it, and you paid them for it. It was considerably cheaper than buying it from the storeroom. We did use the storeroom sometimes, of course, because we couldn't always wait for this bargain price.

About a year after I left the university, I got a bill for four dollars and fifty cents from the storeroom. I really didn't think I owed them a cent because they usually didn't let you have your degree until you paid all your bills. At first I thought, I'm not going to pay it, but then I thought, never mind, I have a job now, I'm making money, I'll pay them the four dollars and fifty cents. And so I did, I sent them a check. A month later I got another bill. This time I wrote a nasty letter. I told them that this bill came from the Comptroller's office, that I had received the same bill last month which I paid, and I had the canceled check to prove it. I didn't think I owed it in the first place, and now they were dunning me again! I never got an answer to that letter. Thirty-five years later, I was invited to Columbia to give a seminar and they took me out to dinner and they were questioning me about the old days, and so I told this story. And the next week, from the current administrator, I got a check for four dollars and fifty cents! [laughter]

GORTLER: The faculty in general was fairly friendly toward the students.

COHN: A bit standoffish. Hammett, for example, was very nice if I came and asked him a scientific question. On that level they were very nice.

GORTLER: Later on you used a method that had been devised by [J. Enrique] Zanetti. Did you know Zanetti when you were at Columbia?

COHN: No. I only knew about him. He had a postdoc that I knew because he was a friend of one of Urey's postdocs that I knew. Just to give a flavor of the times, Zanetti's postdoc was on his sixth one-year postdoc position, each at a different university. And so I knew what Zanetti was doing, synthesizing deuterated compounds. One of the compounds that I knew he had made was deuteromethyl alcohol. So when du Vigneaud asked me to make deuteromethyl alcohol, I decided to go to see Zanetti and ask him if I could do it in his laboratory.

GORTLER: Oh, so you did it at Columbia?

COHN: Oh, yes. I was at Cornell Medical College by that time. I was right in the city, so there was no problem. Zanetti was very gracious. He let me use his equipment. Of course, I bought the carbon monoxide and the deuterium gases that were needed for the synthesis, but he let me use his equipment. I made what would be worth hundreds and hundreds of dollars worth of methyl alcohol. Enough for the rest of du Vigneaud's career! That was the connection. One pretty much knew what other people were doing, I mean what other professors were doing. One didn't feel isolated scientifically. But just as a friendly place, no, it was not.

[END OF TAPE, SIDE 5]

INTERVIEWEE: Mildred Cohn

INTERVIEWER: Leon Gortler

LOCATION: The University of Pennsylvania

DATE: 6 January 1988

GORTLER: During our first interview [15 December 1987], you did not say much about the intellectual climate at Columbia during the period that you were there. Perhaps you could tell me a little bit about that now.

COHN: It was really a very exciting time, particularly in physical chemistry--or chemical physics. Chemical physics was a term which I believe Urey invented; in any case he was the first editor of the Journal of Chemical Physics. Urey disapproved of the departmental seminar in physical chemistry for graduate students. It was essentially a journal club, where the students had to report on current papers in the literature. I have forgotten who was in charge, either Professor LaMer, Professor Hammett or perhaps both of them. Urey didn't think that was a worthwhile kind of seminar, so he started his own in chemical physics. His format in conducting this seminar series was to choose a knowledgeable postdoc, or someone at that level, as leader--not a graduate student but someone above, though not too far above--to draw up a bibliography of a given subject. There would be perhaps ten or twelve weekly seminars in a given research area. We covered such subjects as artificial radioactivity, which had just been accomplished by [Enrico] Fermi; we covered absolute reaction rate theory--[Henry] Eyring had just come out with his theory, and so on. Another subject we covered was isotope-separation--that was Urey's particular research interest. I learned more in those seminars than I did in any courses that I took. They were very good. The person in charge would present an overview. When radioactive isotopes was the subject, Urey imported someone from the physics department to present the overview and draw up a relevant bibliography. The students were supposed to read all the papers, and each student had to present one of them.

By the way, the first seminar that one gave at Columbia as a graduate student was really a baptism by fire. I saw one man, he was about six feet two, a great big fellow, who almost fainted. He kept drinking water. There was a young woman student in Urey's seminar who stopped in the middle, walked out, and never showed up again.

I remember that in the chemical physics seminars, the full professors would sit in the first row--they all came, by the way, Hammett, LaMer and all the senior professors--and then the junior professors, and then the postdocs and then the graduate students in the back. But it was really very exciting, because all the subjects were at the frontier of the field and we went into them in some depth, rather than these journal club seminars which varied from week to week in subject, and subjects were never explored in depth. The chemical physics seminars were like mini-courses, really. It was a very exciting time, because of the fact that Urey was separating the isotopes, Fermi had made almost every element radioactive, Giauque was achieving very low temperatures, and reaction rate theory in chemistry was just being published. We also studied O. K. Rice's work as well as Eyring's, because one of Rice's collaborators, one of his thesis students, Harold Gershinowitz, was a postdoc at Columbia. He had also worked with Eyring, so he was in charge of the series of seminars on reaction rate theory.

Hammett was doing all his very interesting experiments on rates of chemical reactions involving substituted aromatic compounds, basic physical organic chemistry. That was going on at the time I was a graduate student. Also in the physics department, where I took a good many courses, and because of my contact with Rabi, I knew that some very exciting experiments on molecular beams were going on there as well. So there was excitement everywhere. Incidentally, Fermi came over in the summers and used to give courses. I listened in on one of them but I didn't take it for credit.

GORTLER: Was Fermi at Columbia at that time?

COHN: No. He was still in Italy. He came from Italy for the summer. This was 1935 or 1936. So it was a very exciting period to be at Columbia. Of course, a student doesn't quite have the perspective, but when it's exciting, the students sense it. I did want to tell you about the stimulating atmosphere because I remember my years at Columbia with great fondness as far as the intellectual climate was concerned.

GORTLER: I think it's important that you had come away with that, because I know there were other aspects of the experience that you were not quite so happy with.

COHN: That's true. But as far as what was going on there scientifically, it was a very excellent place to be. Also the fact that Urey was so enthusiastic and interested in all these other scientific developments that he wasn't working on himself. He organized the seminar so that these developments could be gone into in some detail. All in all, I had a very good experience there from the intellectual point of view.

GORTLER: Last time we had gotten you into Vincent du Vigneaud's group. Now tell me a little bit about working with du Vigneaud. I noticed that his name appears on almost all of your papers from 1939 to 1947.

COHN: Oh, yes. And he was almost always first author. Except one, he didn't want to put his name on that (8). I don't know why. The omission of his co-authorship made you feel that he didn't respect the work or didn't think it was important. Most of the time I was there I worked on transmethylation, because that had been discovered accidentally through the use of isotopes. I don't know whether you want me to recount that story. It is, I think, a very interesting one, but he himself has written an autobiography called A Trail of Research, where he more or less describes this discovery (9). I was very impressed with his recognition of the underlying mechanism of some very paradoxical experimental results. This is sufficiently interesting, I think, that it should be told, because it influenced my whole intellectual attitude towards science. He had very high standards, he really did, and unless an experiment had been reproduced two or three times, he didn't accept it.

Well, as you know, I was brought to his lab to work with isotopes. He was primarily interested in amino acid metabolism, and in particular sulfur amino acids, methionine and cysteine. There were three experts in this area in the country, of whom he was one. He was interested in knowing how homocysteine substituted for methionine in the diet of the rat. Methionine is an essential amino acid. About half of the twenty amino acids are essential in the diet, that is, the rats can't synthesize them from other metabolites, and one of them is methionine. It had been shown by several previous investigators that demethylated methionine, homocysteine, which is not a natural amino acid, could substitute for methionine in the diet of an immature rat. The criterion of successful substitution was that the rats grew. They don't grow if, say, they are missing one essential amino acid in the diet.

When I came to his laboratory he had synthesized homocysteine with deuterium in the alpha and beta positions (I think it was alpha and beta, but certainly on the beta). The rats were fed pure amino acid diets which, by the way, entailed preparing about ten of the twenty amino acids in the diet, because only about ten or so were available commercially. In the summer the whole laboratory ceased doing research, except me. I was not a synthetic organic chemist. The others either synthesized the unavailable amino acids to be used for the rest of the year, or they isolated them from natural sources. For example, cysteine was isolated from hair, on a large scale, because there were a lot of rats to be fed pure amino acid diets for the rest of the year.

When du Vigneaud designed the experiments, he also added all the then-known pure vitamins to the diets. And the rats did not grow. Now [Erwin] Brand, who was one of the other three sulfur amino acid people--I'm telling you this to illustrate the attitude of the biochemists at that time toward isotopes--he immediately said "It's the isotopes that's doing them in, the deuterium in the homocysteine." They were very suspicious of isotopes, and they didn't want to accept the use of them as harmless. Du Vigneaud, of course, immediately tried homocysteine without any deuterium, and the rats again didn't grow. Now, [William C.] Rose of the University of Illinois was doing the same type of experiments, and his rats were growing. So du Vigneaud, who was then at George Washington University, sent the rats from Washington, DC, to Urbana, Illinois, and the Urbana rats arrived in Washington. The Urbana rats did not grow in Washington, and du Vigneaud's rats did grow in Illinois.

Du Vigneaud then looked carefully at the protocols to see what the difference was between the two experimental protocols. They were both feeding pure amino acids, but when it came to the vitamins, du Vigneaud was using pure samples of the various vitamin B's, but Rose, as a source of vitamin B, was using something called "tiki-tiki"--rice polishings containing all the vitamin B complex. Du Vigneaud noticed that and immediately said, "Choline. Transmethylation from nitrogen to sulfur." As a consequence he added choline to the homocysteine diet, and the rats grew. I thought that his immediate realization was a remarkable feat. I was there when he did it; it was amazing. First of all, choline isn't usually considered a vitamin because it's present in the diet in fairly large amounts. But he knew that tiki-tiki had choline in it and he, of course, knew that choline was an N-methyl compound, and he immediately made that mental jump. He then did experiments to test his interpretation, and indeed, it proved to be correct. That was the discovery of transmethylation in animals. One interesting aspect from the viewpoint of the historical development of metabolism as he later pointed out himself in discussions with me, (I don't know if he has ever stated it in print), is that if, at that time, one had known all of the vitamins, he would never have discovered transmethylation. If the vitamin folic acid is in the diet, the rat can synthesize methyl groups from C-1 fragments. Since folic acid had not yet been discovered to be a vitamin, it was not present in the diet used so that methyl groups could not be synthesized by the alternate C-1 pathway.

I was assigned the task of making deuteromethyl alcohol. I think I told you earlier that I went to Zanetti's lab at Columbia and made the deuterated compound from carbon monoxide and deuterium gas at 10,000 pounds pressure.

GORTLER: Yes. I was going to ask you about that paper (10). That's a major paper that you had with du Vigneaud. You made the deutero alcohol, and then you showed that...

COHN: Then other members of du Vigneaud's group converted the alcohol to methyl iodide, and from that they synthesized (CD_3) methionine and $(CD_3)_3$ choline. Du Vigneaud only experimented with whole animals, so that he couldn't determine the intermediate steps. It was [Guilio L.] Cantoni who later discovered that the true methylating intermediate is S-adenosyl methionine (11), and to this day it's the central compound of transmethylation, the methyl donor for creatine and choline as well as the source of the methyl groups on nucleic acids, for example. It's a very important compound because it methylates everything that has to be methylated. There are other methylation pathways, however. There are C-1 fragments that can serve as precursors of methyl groups, but transmethylation is the main pathway of methylation in the body, and methylation is very important in the function of many biological processes. The methyl group can make the difference between an active and an inactive substrate in an enzymatic reaction.

Most of the years I was with du Vigneaud I worked on transmethylation, because then he extended the study to establish whether the methyl group, not only of choline but also of creatine, was derived from methionine. And it is; and the methyl group of anserine as well, and so on. He isolated a number of known methylated compounds in the body and found that the deuterium labeled methyl group of methionine that was fed ended up in all the compounds examined. All these experiments were done in rats, and so I spent eight and a half years of my life working with rats. However, I did all the deuterium analyses, and I participated in planning the experiments, so that the isolated product would contain an amount of deuterium sufficient to be detected.

GORTLER: The analytical method must have been extremely tedious. You had to isolate the compounds, and then burn the compounds, and isolate the water...

COHN: ...purify the water, and then measure its density. You couldn't do more than two, at most three analyses a day, because of the combustion and purification procedures. Even after the compound was isolated, you understand, that was no easy task.

There's another metabolic pathway that he was interested in. There are two naturally occurring sulfur-containing amino acids; one is methionine, the other one is cystine. Cystine is a non-essential one, that is, from the dietary point of view, but from the viewpoint of the body, cystine is as important as methionine. He was interested in how the methionine was converted to cystine. Since cystine is non-essential, that is, it can be synthesized in the animal body, its sulfur obviously must come from methionine. Was the whole carbon chain used, or just the sulfur? And so du

Vigneaud assigned the problem of synthesizing methionine labeled with ^{34}S and ^{13}C to a postdoc, who was a good organic chemist. You must realize at that time there was no tritium or ^{14}C available. Maybe about the time we did that experiment they had just been discovered, but they certainly were not available. It took a year to synthesize that compound, and then we had to feed the compound to the rats. By the way, we fed the diet by stomach tube; we weren't going to let them slop around with this valuable compound. The rats were shaved before the experiment, and then they were fed the labeled methionine. The new hair that was grown was shaved off after there was enough of it and the cystine was isolated from the hair, and then that cystine was analyzed. It was really a beautiful experiment. All the sulfur came from methionine and none of the carbon (12).

There was a real intellectual pleasure in doing these kinds of experiments because they yielded a 'yes or no' answer. Either A went to B or it didn't go to B. But, you had to have the temperament for this kind of experimentation because some of these experiments lasted months before you got the answer. Also, think of the patience involved in waiting a year for the synthesis of the compound, then months to feed it, followed by isolation from the animal, then analysis for the isotopic composition. ^{13}C and ^{34}S had to be analyzed on a mass spectrometer and I went to Rittenberg's lab, where he had a mass spectrometer, to do the analyses.

GORTLER: You didn't want to make a mistake after all this effort. [laughter]

COHN: These were experiments where you didn't make mistakes. Du Vigneaud was also working on peptide hormones of the posterior pituitary; one was called vasopressin or pressor, and the other was oxytocin. He was awarded the Nobel Prize for his sequence determination and synthesis of both compounds. He synthesized the first biologically active polypeptide hormone, and that's what he got the prize for. At the time I was in his laboratory, before 1946, the exact composition of these hormones was not known because they were not available in pure form. We used to assay them biologically. Du Vigneaud wanted to know the isoelectric point for vasopressin, so I devised an apparatus for measuring isoelectric points. He had beef and hog vasopressins, and I found that there was a difference in isoelectric point of almost two pH units between the two. I had plenty of the beef material, but the hog hormone was rather rare. Hundreds of pituitaries had to be used to get enough material to work with. He wouldn't let me publish the hog results, because I had only done it twice. I didn't have enough material to do the experiment more than two times. But we did publish the beef results.

There is an amusing sequel. Many years later, after he had received the Nobel Prize, he gave a lecture at an international meeting. By this time, they had purified the vasopressins and had redone the isoelectric points. The hog and the beef compounds differed; one of them contained lysine and the other one had arginine, and that was the reason for the isoelectric point difference. After the lecture, I went up to him and reminded him that I had found the different isoelectric points, I don't know how many years earlier. He really didn't remember. I said, "Well, you have my notebooks. You can look it up." When one left his laboratory, one left all notebooks. That was before the days of duplicate notebooks. Now there are notebooks with carbon paper, so you and the boss can each have a set. After that lecture he always mentioned my early work in his lectures. [laughter]. Anyhow, that's just an amusing sidelight.

I was in a very special position in his laboratory because I was the only physical chemist there. All the rest were organic chemists or biochemists, but I was the only physical chemist. So I was asked to do all kinds of things that I didn't know how to do. [laughter] Their notion of what a physical chemist should know included how to change the telephone lines (he had an internal telephone system), how to fix the Leeds and Northrup galvanometer, and so on. But they soon learned that a physical chemist didn't necessarily know how to do all those things. Anyhow, intellectually I had a very fine time there. I didn't realize until I left that when you're a member of a team, nobody realizes that you exist or that you have contributed anything. After four years in du Vigneaud's lab I had been offered a job with much more independence. After I had accepted, it was withdrawn when the person who had offered it to me found that du Vigneaud didn't want me to leave.

GORTLER: He had a good deal of control over what happened to his people.

COHN: That's right. He was very paternalistic and very concerned, but also very possessive. He once said to me, "I don't know why these people want to leave." He kept his Ph.D. students at least one year afterwards as postdocs. He had a habit of keeping postdocs (I stayed there almost nine years), because he said they were valuable. He said, "[Otto Heinrich] Warburg used to keep people twenty years." This was in Germany, of course. But he did believe that I should follow my husband around, so when my husband accepted a job in St. Louis, at Washington University, he was very helpful. He wanted to help me get a position in St. Louis. When Carl Cori was in New York for a Harvey lecture six months before I was to move to St. Louis, du Vigneaud invited Cori to have lunch with him, and me too. So I met Cori on that occasion, and du Vigneaud introduced me as his right-hand woman who had been with him for eight years. Cori turned to me and said, "Where have you been these eight years?"

At that point it suddenly hit me that I was an unknown. After having worked in this field for eight years, nobody knew that I existed.

GORTLER: Just another name on the paper.

COHN: Yes, by that time I had co-authored about eleven or twelve papers. Du Vigneaud also had a policy that nobody gave a talk at a meeting except himself. Actually, in some ways that's good, because young persons going to meetings now rarely hear the established scientists speaking.

GORTLER: True, true.

COHN: You very often hear incomprehensible postdocs, foreign postdocs who speak English poorly, or you hear a graduate student. You very rarely hear the top people give talks at meetings, except plenary lectures, but not research talks on current work. That wasn't the case in the thirties and forties, at least not in the Society of Biological Chemists. The top men, and women occasionally (there were very few), used to give talks. Once he did allow me to give a talk. I don't know why. It was an invited paper which he and I co-authored, and he let me give the talk. But that was an exception to prove the rule.

GORTLER: During that period you also had one paper with Fritz Lipmann (13).

COHN: Oh, yes. Fritz Lipmann came over for a two year stay in du Vigneaud's laboratory. Du Vigneaud was very anxious to work on a level other than the whole animal, i.e., tissue slices, enzymes, and so on, but he had no experience, and Lipmann, of course, knew all about those things. He was an enzymologist, he knew how to work with tissue slices, he knew how to work with extracts and with pure enzymes. It was Dean Burk, whom du Vigneaud thought very highly of, and who came with him for a two year stay when du Vigneaud first went to Cornell, who suggested Lipmann. Burk was then at the National Cancer Institute, I believe, and he had known du Vigneaud in Washington.

GORTLER: Where was Lipmann before?

COHN: He was in Denmark at the time. He had left Germany, and he was in Denmark, but he didn't have a tenured position. He came in about June 1939, and then the war broke out in September, and he couldn't go back. He had planned to stay for two years.

In any case, he was in du Vigneaud's laboratory for several years, and then he left.

[END OF TAPE, SIDE 1]

COHN: At that time a very interesting finding had been published by Kögl that there were D-amino acids in cancer tissue (14), rather than L-amino acids. That was such an unexpected and novel finding that almost everybody in biochemistry who worked with amino acids tried to repeat it. If it was really true, it was sensational. Well, it turned out that it was a fraud, not on Kögl's part, but his technician had done him in. Among many others, Lipmann was trying to either prove or disprove the result. One of his experiments involved an isotope dilution method of analysis using deuterium; that's why I came into the picture. Nobody, by the way, could confirm Kögl. It was found by some very careful workers in the course of checking the results that when you crystallized the particular amino acid which he had isolated, that you did get a slight preference of one isomer or the other depending on the conditions of crystallization. But that was true whether you got your starting material from normal tissue or from cancer tissue. By the way, Kögl never withdrew his finding. He didn't believe that his technician had perpetrated a fraud. [laughter]

GORTLER: That's one of the beauties of science, that other people can check your work.

COHN: Yes, and even though nobody could confirm it he wouldn't withdraw his finding. I remember Dean Burk, who had a flair for language (or at least, thought he did), held a seminar which he announced as "Köglism and Neo-Köglism." [laughter]

GORTLER: You had a paper that did not have du Vigneaud's name on it. That was with W. H. Fishman (8). Was that the one that he would not put his name on?

COHN: Yes. I don't know why.

GORTLER: You did a comparison of acetylation of phenylaminobutyric acid with p-aminobenzoic acid and sulfanilamide.

COHN: In fact the symposium where I presented the joint paper with du Vigneaud was on acetylation. I don't know why he didn't want to put his name on the paper with Fishman, but he didn't.

You can't imagine a greater contrast than that between du Vigneaud and Lipmann. Lipmann was completely intuitive and couldn't tell you how he arrived at his conclusions. It was as though it came to him from on high. Du Vigneaud, on the other hand, always pointed out to us, the younger people, exactly every step in his reasoning.

GORTLER: It sounds as if it was a good atmosphere in which to learn how to do science.

COHN: Oh, yes, because du Vigneaud was very explicit. But Lipmann, even if you questioned him, couldn't explain ideas to you. He was very inarticulate.

GORTLER: I see.

COHN: But it was during those years, when he was in du Vigneaud's lab, that Lipmann wrote the famous paper on so-called high-energy phosphate bonds (15). The whole idea that ATP [adenosine triphosphate], for example, and other compounds like phosphoenolpyruvate were a special class of compounds whose phosphate bonds were different from ester bonds and which he designated "high-energy" and pointed out their importance in the bioenergetics of the cell, really had a tremendous influence on the field.

GORTLER: So you were aware of that kind of thing before you left du Vigneaud.

COHN: No. I wasn't even aware of his paper.

GORTLER: When did your interest in phosphorylation begin?

COHN: Well, that happened when I got to Cori's lab. That's when I discovered Lipmann's paper--not earlier, because he was very reticent. He did think about a great many things. For example, he said to me one day, "Why don't you try to see if the methyl group of creatine comes from methionine?" I mentioned this to du Vigneaud, and told him that Lipmann had suggested this. He said, "Of course. This is one of the experiments I have planned," and I'm sure it was. But Lipmann was sufficiently interested, you see, in what was going on in other labs to comment. I certainly wasn't aware that he was writing that paper, and in fact it was only after I got to St. Louis that I was made aware of it and that I read it. He wrote it in 1941, I believe, and it was 1946 when I went to St. Louis. But there was no interest in phosphate compounds in du Vigneaud's laboratory at all. As I told you, the focus was on sulfur compounds, methylation and acetylation.

GORTLER: You went to St. Louis because your husband got a job, and in St. Louis you were a research associate. How did you get paid? Cori paid you?

COHN: Yes, of course.

GORTLER: But things were quite different there. You must have had more freedom.

COHN: Oh, certainly.

GORTLER: You were the senior author on your papers. Cori's name seldom appeared on your papers.

COHN: Absolutely.

GORTLER: Did you negotiate that, or was that just the way their group worked?

COHN: No. After all, I had been on a team for almost nine years, and I didn't want to do that again. When I had the first discussion with Cori in New York, I told him some of the problems I would like to work on. I still remember what the problems were. One was the use of ^{18}O to determine bond cleavage in enzymatic reactions and the other was to use deuterium and tritium to measure the isotope effect in enzymatic reactions. After that interview, I didn't hear from him for a long time. I didn't know whether I would have a job or not. I later found out when I got there that the reason he hadn't done anything about it was that he and Gerty Cori were offered jobs and were seriously considering leaving St. Louis. I remember this very well because I said to my husband, "What am I going to do if I get there and I don't have a job?" My husband had great confidence in me. He said, "Well, we have a little money saved up. You can work without pay for a year, and by that time I'm sure they'll give you a job." Anyhow, we didn't have to do it that way because Cori did offer me a job.

GORTLER: Did you have children at that time?

COHN: I had two. I had two children while I was working for du Vigneaud.

GORTLER: That was the next question I was going to ask you. How did you manage to juggle all this?

COHN: Well, it wasn't easy. I had to hire people.

GORTLER: You and your husband were running two careers, and you were raising children, and you hired people to...

COHN: To look after my children. It was not easy, because my first two children were born during World War II. To get domestic help of any kind was very difficult. I did it, but it wasn't easy.

GORTLER: You had two early papers that had the Coris' name on them (16). I suppose those were sort of introductory papers.

COHN: No, no. Actually, I was working on the first paper that I published by myself simultaneously that I collaborated with Gerty Cori (17). I had presented two possible research problems to Cori and he preferred the ^{18}O problem. So I told him that I would have to build a mass spectrometer if I was going to do ^{18}O work, and he agreed. He supplied the money for it, and he also supplied an electronics man to help with the circuits and so on. And so I built one. When I first came there, they tried to get me to work with them. Gerty particularly, she was a very enthusiastic person. She would come and tell me all the wonderful problems they were working on, and I would just say, "No. I want to do my own thing." Well, they were very smart people, so after a few months of this they realized I really meant it and they just left me alone. So I went ahead on my own. Once having established that, I was quite willing to collaborate with them and did so (16).

I also set up a radioactive isotope laboratory for them. In 1946 commercial instrumentation for measuring radioactivity became available. We did a little bit with radioactive sulfur in du Vigneaud's laboratory, and at that time we had to build our own Geiger counter. I think in 1946 in St. Louis I still had to have the shop build me a Geiger counter. But a commercial scaling circuit became available to do the actual counting. It was very new. A lot of electronic instruments came out of Los Alamos, and many companies went into business when the circuits were made public. I remember that I bought a scaling circuit from Nuclear Chicago, and I would call them every few days to tell them this didn't work or that didn't work. They'd say, "Try this. Try that." And then I realized that I was doing research for the company. Finally I said, "When you get all the bugs out of this thing, you can send me one. I'm sending this one back." That's what it was like in those days.

At the same time I started building the mass spectrometer. Al Nier from Minnesota was great. He supplied me the main part, the tube with the ion chamber, which he had built in his lab. He also allowed his mechanic to wind the magnet for me. The problem of getting copper then was very difficult. In general, it was very difficult to get materials at that time.

GORTLER: This is already after the war.

COHN: Yes. This was right after the war. It took a couple of years till they caught up, that is, till things were easier. A year at least.

At Cornell, I also assembled a mass spectrometer, and I needed a tube at that time, too. Harry Thode, [who was] in Canada, had been a postdoc in Urey's laboratory when I was a graduate student. He became not only the head of the chemistry department at McMaster University, but he became president of the University. I think he's still alive. The last time I saw him was at an ACS meeting about five years ago. I knew that he was building mass spectrometers during the war. So I got in touch with him and asked him if he would give me a tube. He said yes, and he sent it to me, but it was only partially finished. I had to finish it. This tube was made of glass--but it had to have a metal sleeve on the inside. That was needed to conduct the ions that hit the walls. He had used stovepipe made of non-magnetic nichrome V. And I decided that I'd use Greenfield cable made of nichrome V. I had the nichrome V. I phoned several companies in New York that made Greenfield cable, and they'd say, "Say, lady, don't you know there's a war on?" and refuse me. I decided to go to the source and contacted Anaconda Copper. They did it for me and refused to take any money for it. So, when I was in St. Louis and had trouble getting copper from local suppliers, I just called Anaconda Copper again, and I got it. The big companies do this just for good will, and so I learned my lesson. You go to the top. I managed to get all the materials I needed that way. The mass specrometer I built in St. Louis was a very good one. The one that I built at Cornell never worked well, but the one in St. Louis was excellent. I used it the entire time I was there, from 1947 when it was completed until 1960 when I left.

GORTLER: Perhaps at New York, you didn't have that much need, because there were all these other mass spectrometers around that you had access to.

COHN: No. During the war, Nier had been improving the design of mass spectrometers. His design, in 1946, was very much better than the one I had used at Cornell. For example, at Cornell I actually used storage batteries for the voltage supply, because they hadn't designed a power supply that was stable enough. But, during the war, Nier had perfected an isotope ratio instrument and fortunately, I knew Al Nier. He had the tube and the magnet made by his machine shop and that was, of course, a great help. But at Cornell I had to do much more myself. I had to get the metal sleeve, I had to make all the metal-to-metal and metal-to-glass seals. Thode had sent me the ion chamber, which was most generous of him in the middle of the war, and I had to use my ingenuity for the rest because there really weren't facilities available at Cornell Medical College to make such instruments. I had friends among physicists and engineers, which was helpful.

GORTLER: You've always seemed relatively comfortable around large instruments. This goes on through your entire career. Do you think you inherited some of that from your father? You said that your father was terrible with his hands but, on the other hand, he did invent a machine for cutting trousers.

COHN: Yes, but he was very inept. He couldn't do anything manually. I'm pretty good at glassblowing. I could put circuits together, too, solder and so on.

GORTLER: Where do you think that capability came from?

COHN: Probably my mother. She was exceptionally good at embroidery and knitting.

GORTLER: At what point in your career did you pick up these skills and become comfortable with instruments?

COHN: Oh. Always. Don't forget that the job I had for two years after I had my master's degree was with engineers, and instrumentation was very important there. I got an appreciation of machine shop work and all the rest on that job. I devised my own equipment there, except for the recorder. They had an instrument section that did nothing but design instruments. I told them what I wanted, and they designed it.

GORTLER: How would you characterize the differences between the laboratory at Cornell and the one at Washington University in St. Louis?

COHN: They were very, very different. Du Vigneaud's was a one-man show. This was not atypical, by the way, of medical schools at that time. The big shock came when I went from a university chemistry department to a medical school, because most medical school departments had only one full professor, the man at the top. I wasn't used to that. At the Columbia chemistry department there were quite a few full professors. Du Vigneaud didn't even have an associate professor in the department. He had two assistant professors whom he had inherited. The associate professor whom he had inherited left. One of the assistant professors, who stayed there a while, left too, about four or five years later. And the other assistant professor was brought into the group. So it was definitely a one-man department.

GORTLER: This was now the Department of Biochemistry?

COHN: Yes. It was the Department of Biochemistry of Cornell Medical College. And everyone worked as a team. In St. Louis it wasn't like that at all. First of all, there were Carl and Gerty, his wife, who worked together. They also worked separately with postdocs. Du Vigneaud had a limited number of graduate students, because there were no courses for them to take in the Medical School. Cornell University was far away. So he wouldn't take anyone without a master's degree in chemistry.

In Cori's department they had even fewer graduate students. There was perhaps one per year. It was hard to be a graduate student there, because you were treated like a postdoc. There was no group of graduate students, so the only group were postdocs. So that was a difference.

There was a very great difference in style. Even if people worked with Carl Cori or with Gerty Cori, there would be two or three names on a paper. Each postdoc worked on a different problem. It wasn't the kind of joint team work, an assembly line of experts that du Vigneaud led. The assistant professors in Cori's department were all independent. Cori once told me his philosophy of leading a small department. He didn't try to cover all of biochemistry in the department. The department only covered carbohydrate research, and he covered everything from enzymes, including isolation, purification and physical aspects of the proteins, to physiological studies. That is, there were people in the department who covered these areas. But he wanted a department where everyone could talk to everyone else. Rather than having someone working on nucleic acids and someone else working on lipids and so on. As far as the research was concerned, he believed that if you had a small department (there were only about nine faculty members), you choose the faculty so that everyone was investigating different aspects of the same area. That was his philosophy. But the assistant professors certainly were completely independent, though they worked in an area that he was interested in. Since he had purified so many enzymes, if they were interested in the physical or kinetic properties of enzymes, they usually worked on those enzymes, because the material was available.

The laboratory in St. Louis was very international. People from all over the world came there. One of the reasons was that, first of all, it was a very outstanding laboratory, but another reason was that in 1946, when the war was over, many of these foreigners didn't have any place to work. Their labs were destroyed or certainly unusable. So they came to this country for a year or two, and it was like a U.N. there, as far as the background of the people was concerned.

GORTLER: Who was providing support?

COHN: Du Vigneaud's support came from the Rockefeller Foundation originally, and when I left, he got a grant from the American Cyanamid Company with no strings attached; half a million dollars. That was 1946, when that amount was a small fortune.

Cori never told me, but I was told that he got his money, most of it, from Eli Lilly. He was interested in carbohydrate metabolism, insulin, diabetes, and so on, which of course Eli Lilly was interested in. And I was told that they sent him a personal check every year for $100,000. I should also tell you that at that time Washington University Medical School was really quite a remarkable place. They put research ahead of everything else in that school, and had for many years. They had a so-called full-time system in the clinical departments, that is, the clinical faculty worked for salary. They didn't collect from patients, the school did. And twenty percent of the take of the clinical departments was turned back to the pre-clinical departments for research.

GORTLER: An enlightened administration.

COHN: It was an unusual place. They really agonized over appointing even an assistant professor. The chairmen of all the departments formed the executive committee, and they actually used to read the publications of the candidates. The executive committee decided whether a candidate could be hired as assistant professor in every department. They believed that's how they could keep up standards.

GORTLER: You've mentioned the fact that people in du Vigneaud's group were like a team, and I noticed that almost all the papers you had from there also listed a fellow by the name of Joe Chandler.

COHN: Yes. He was the assistant professor who was "gleichgeschalted," as I used to say.

GORTLER: And Sofia Simmonds?

COHN: She was a graduate student. She's Joe Fruton's wife.

GORTLER: Oh?

COHN: There's a book on biochemistry by Fruton and Simmonds (18).

GORTLER: Fruton and Simmonds, of course. I never made that connection.

COHN: Joe worked across the street at Rockefeller Institute at that time.

GORTLER: Did any of your children go into science?

COHN: My son. My daughters get annoyed when I say they're not scientists. They're both psychologists, but they're clinical psychologists. My son got a Ph.D. in biochemistry. He's now an associate professor at the University of Connecticut Medical Center. He happens to be in the physiology department and he's now a cell biologist, but he got his Ph.D. with Paul Berg at Stanford in biochemistry.

GORTLER: Did you discuss scientific problems with your husband?

COHN: Occasionally. Our fields are fairly far apart; he was a theoretical physicist who worked primarily in elementary particle theory for the last twenty years of his life.

GORTLER: Yes. But you collaborated with people in physics departments.

COHN: Yes. I found out about NMR and EPR because of the fact that my husband was in a department at Washington University where research in magnetic resonance was very actively pursued.

I certainly consulted my husband if I wanted to know anything in physics. He was most knowledgeable about physics, he was rare in that he knew all fields of physics. The graduate students here loved it. For a few years he gave a course before they took the qualifying exam, on the highlights of physics covering the whole field. He had taught every course in the book. So he was an excellent person to use as a consultant, and I never hesitated, if I had a problem, to ask him about it. In recent years he would say, "I don't know anything about NMR." He said that, but in fact he published a very fundamental paper in statistical mechanics on the equation of state that had, as an example, NMR (19).

GORTLER: Your first solo paper from Washington was almost a classical physical organic paper on the hydrolysis of glucose-1-phosphate (17).

COHN: That's right. That, by the way, was called the "Cori ester." They had discovered and characterized that metabolite, glucose-1-phosphate.

GORTLER: You used both acid and enzymic catalysis. Tell me a little bit about the origins of that work. I mean, you'd obviously thought about it before you went to St. Louis.

COHN: Yes. As I told you, my thesis work was on ^{18}O, and at the time there were many organic reactions whose mechanism I thought one could learn something about by using ^{18}O. Of course, I knew that the Cori laboratory specialized in enzymes. They were the outstanding enzymologists in the country. When I went there, I thought, here's my chance to apply this to biochemical reactions, that is, to enzymatic reactions. That was the origin of it, and Cori was very pleased with the problem. He was also interested in mechanism. I started reading their papers and I realized that no one knew whether the C-O bond or O-P bond of glucose-1-phosphate was split when it was converted to glycogen in the reversible reaction catalyzed by glycogen phosphorylase. Actually, it has since been found out that it functions in the breakdown pathway of glycogen, not in the synthesis. At the time it was thought to be the pathway of synthesis.

[END OF TAPE, SIDE 2]

COHN: I thought it would be very interesting to compare the enzymatic with the non-enzymatic cleavage. I knew by that time that enzymes were highly specific, so I figured there would be only one pathway with an enzyme. I told Cori about this, and he was sufficiently interested to finance the construction of a mass spectrometer. That was the only way I could do this problem. I not only had the problem of assembling a mass spectrometer, but of devising a method of converting the oxygen of phosphate to CO_2 so that its isotopic composition could be determined by mass spectrometry.

GORTLER: Your method seems simpler than most of the other methods you had used before.

COHN: The disadvantage of the method that I devised, which was the dehydration of KH_2PO_4 with subsequent equilibration of the water with CO_2, is that you only get one oxygen out of the four in the phosphate. Presumably it was the average, which I think it was. Nevertheless you had to use more material than was desirable, because you had to have enough water to handle. Later, I devised another method. I used the reduction of solid phosphate with carbon at about 1300°C. It was not easy to devise a way of doing that. But I did prefer this method, because first of all I got all the oxygen, and secondly the immediate product was a gas, carbon monoxide. The method had the disadvantage that carbon monoxide has the same mass as nitrogen, and you had to be very careful never to allow any air into your system. You really had to maintain a good vacuum throughout the experiment. Reaching 1300° or 1400°C and handling the materials required a good deal of ingenuity. The initial method that I developed, the dehydration of KH_2PO_4, was easier to perform than the later one but I did use this second method, because I could then work with smaller quantities of material.

GORTLER: And then in the first method you had to exchange the water with CO_2.

COHN: You had to get the CO_2 in known amount and exchange with water. I had done that part in my thesis, the water-CO_2 exchange. So once I got water I knew what to do with it.

GORTLER: You must have gotten a great deal of satisfaction out of that particular problem.

COHN: Yes, it sort of had been in abeyance for about nine years. This was something I had wanted to do nine years earlier. But it was all right, I didn't mind. I am very adaptable. I got quite interested in the transmethylation problem. It was a very interesting problem.

GORTLER: For a short period, you were at the Harvard Medical School.

COHN: Yes, for one year. My husband was invited to MIT for a year. Professor [Victor F.] Weisskopf was going off to Europe, to CERN, I believe, and they asked Henry to take his place for a year. I had just said no to a job he'd been offered at Carnegie Tech, because there was nothing for me in Pittsburgh at the time. I felt very badly about Carnegie Tech. I visited Pittsburgh and talked to Klaus Hofmann, who was at the University of Pittsburgh, and whom I knew from du Vigneaud's lab. Klaus said, "There isn't a job for you now, but in a few years there will be." Well, I didn't want a hiatus of a few years.

If you're interested in one aspect of Cori's diplomatic talents, I'll give you an example. My husband was offered a job at Westinghouse in 1948, two years after we came to Washington U. He wasn't even interested in visiting or considering it. I said, "Why don't you go and look at it?" He came back wildly enthusiastic. First of all, they had offered him double the salary he was getting at Washington University, and secondly, they told him he could do anything he liked. He didn't have to work on any company problems. They just wanted him for window dressing. Well, that sounded very attractive to him, because he'd have all his time for research and he could do what he liked. So, he told the chairman of his department, a very, very correct Englishman, who wrote a letter to the Provost. The Provost had, just before that, come out with a policy that the school would not react to outside offers. So a week or two later, Henry met the Provost on the campus, who said, "Nice to have known you, Mr. Primakoff." Henry came home and told me, we were going to Pittsburgh. What else could we do under the circumstances? So I went in and told Cori that we were leaving. He was just astounded. He said, "Why?" I told him the whole story. He said, "Do you want to go?" I said "No, I don't want to go." He said, "Professor [Arthur L.] Hughes (that was the chairman of the physics department) never should have written a letter. What could the Provost do? He couldn't go back on his word. Do you mind if I handle this?" I said, "Not at all." So he called up Hughes and said, "Rules. There are always exceptions to rules." They both went to see the Provost--because the chairman of Physics didn't want Henry to leave either, you understand. As a result of their visit, the Provost decided that Henry would get a raise, not a very big one, but he would get a raise. A friend of ours who was in the physics department, who had come at the same time Henry had, would get a similar raise, though he had no outside offer. That made it okay as far as the Provost's principle was concerned, and to sweeten it, they were going to raise my salary. When I told Henry all this, or when his chairman informed him of it, and when he thought it over, he decided he really didn't want to go to work for Westinghouse, so we stayed.

It was because of the Carnegie Tech offer and the Westinghouse offer that I thought, "Oh, well, I can't say no again," and so we went to Boston. When I told Cori that I was going to Boston for a year, he said, "I'll call [A. Baird] Hastings," who was the chairman at Harvard. Consequently Hastings offered me a job for nine months.

GORTLER: But he also let you do your own work.

COHN: Oh yes, he let me--but he also paid me peanuts. [laughter] I was shocked. And then I found out that the assistant professors weren't getting any more than I was.

GORTLER: They couldn't very well pay you more than the assistant professors.

COHN: You know what an assistant professor in the Medical School at Harvard earned in 1950? I'll tell you what I earned and they weren't earning any more--$300 a month. That year I earned $2700 because I only worked nine months. That was low even then. After all, it was 13 years since I received my Ph.D.

When I left du Vigneaud's lab, I was going to be earning $4250 the next year. That was in 1946. I took $500 less from Washington University. But four years later, $300 a month was low! And the assistant professors were earning no more than that $3600 per year. You were paid with prestige at Harvard. [laughter]

GORTLER: You can't eat it, unfortunately.

COHN: No. Henry was getting a good salary at MIT, so it didn't matter that I was earning so little.

GORTLER: The next paper you told me was important was one that you had worked on partly at Harvard, and that was on oxidative phosphorylation (20). Tell me a little bit about that work and why you thought it was important for you.

COHN: Well, there was a very interesting colleague in the department in St. Louis, who told me in no uncertain terms that this work I was doing with ^{18}O with these enzymatic reactions wasn't really very interesting because everyone knew what happened in those reactions. Actually, the glucose-1-phosphate problem was important because it showed that the reaction was a glycosyl or glucosyl transferring reaction, rather than a phosphoryl transferring reaction, when the cleavage occurred between the C and the O. He said, "What you should do, is go into completely uncharted waters, and really attack a problem that nobody knows anything about, like oxidative phosphorylation." So I thought about this for a while, and decided he was right.

GORTLER: Who's the guy who told you this?

COHN: His name was Graham Webster. He was a very imaginative man. I did an initial experiment at Washington University, and found that something very exciting happened, that the phosphate exchanged with water. There was a professor by the name of Ed Hunter in the pharmacology department who was working on oxidative phosphorylation, and so I went to him. I did the first experiment with mitochondria that he had prepared. It really was a very exciting result; in no enzymatic reaction had I ever seen an exchange of phosphate with water. The oxygen phosphate doesn't exchange with oxygen of water at a measurable rate at 25°C. At 100°C and pH 4.5 it takes about seven days for the oxygen to equilibrate. In mitochrondria the exchange was occurring, of course, at room temperature and rather rapidly. So I realized that I had something interesting to follow up although not what I had originally planned. I remember before I left St. Louis I told Cori about it, and I said, "I'm going to spend a year trying to figure out what's going on." And he said, "Good. If you do find out something, you'll make David green with envy." David Green was a big shot in the field of oxidative phosphorylation.

When I got to Harvard, I decided to pursue this problem further and I went to see Wayne Kielley at Tufts Medical School. He was a first rate scientist who worked in the field of oxidative phosphorylation and he taught me how to make mitochondria. The next obstacle was that I needed a mass spectrometer to measure $^{18}O/^{16}O$ ratios. A. K. Solomon in the physiology department, who was a biophysicist, had a spectrometer of the same kind that I had in St. Louis--which, by the way, was later sold commercially under the name Consolidated-Nier. Unfortunately, he didn't have it operating as an isotope ratio instrument as it was designed to operate. It was a dual receiver instrument, so that you could get isotope ratios very accurately, because any instrumental variation affected both isotopes the same way, a change in the electron current for example. But he didn't have it working in that way, because he was investigating deuterium and hydrogen, and they're too far apart in mass to accommodate with dual receivers, so he used a single receiver only. They had never gotten the second receiver working. I spent some time with his electronics man, getting the mass spectrometer to operate as an isotope ratio instrument. Finally, it did work, and since I had learned how to make mitochondria, I could proceed. When I came back to St. Louis, I remember telling

Cori how proud I was of the fact that I had learned to make mitochondria that retained their ability to carry out oxidative phosphorylation, and he just laughed. He said, "Here you are constructing mass spectrometers, and you're proud of the fact that you've prepared viable mitochondria." It's all a matter of viewpoint, you see. [laughter]

GORTLER: If you had always been making mass specs I guess you thought nothing of it.

COHN: But mitochondria were another thing, because in fact it was difficult to prepare active mitochondria. Interesting, the history of such systems. The mitochondria that were prepared in the late 1940s were never really completely intact. Several years later, everybody started making intact mitochondria. Everyone in the field contributed some improvements, and suddenly everybody's mitochondria worked. The trouble with the ones that weren't intact was that they had an ATPase activity which hydrolyzed ATP, the product of the reaction. That's how I got started on oxidative phosphorylation, and it is a fascinating problem which I never solved, though I worked on it for quite a number of years. I did find out a number of things, but I never really found out how oxidative phosphorylation worked. But Paul Boyer out at UCLA has continued on the ^{18}O phosphate exchange, and he has taken it much further than I ever did, and obtained some mechanistic information from it, particularly from the distribution of the four oxygens.

GORTLER: So he knows more about why exchange is taking place so rapidly.

COHN: He has established that there is more than one step in which phosphate oxygen exchanges with water. He knows, for example, that depending on the distribution of the different species of ^{18}O, if you can fit that to a one-process mechanism, you know that there's only one step in which this happens, but if it can't be fitted at all, that there are two or more steps. This is an example of the kind of thing he has found out from the distribution of phosphate containing four ^{18}O, three ^{18}O, two and so on.

The observation that really pleased me, though, came much later. It was here [at Penn], where I found that I could analyze the concentration of ^{18}O in phosphate by NMR (21), and obtain directly the distribution of the five possible ^{16}O, ^{18}O species of PO_4. I'd sort of brought together all the methodologies that I had ever used. You have to do some very complex chemistry to obtain the information by mass spec.

GORTLER: Yes.

COHN: As you can well imagine, it's not an easy task. But with NMR, it's all spread out in the spectrum for you.

GORTLER: Yes. There were three of those papers that you starred for me, and I'll try to get back to those. In 1954, you published the first of a good many papers using electron paramagnetic resonance [EPR]. You published this with Jonathan Townsend from the physics department at Washington University (22).

COHN: Yes, he had constructed the spectrometer.

GORTLER: How were you introduced to this new technique?

COHN: I was interested in enzyme mechanisms of kinases. I was still doing work on oxidative phosphorylation, but I was also doing work on enzymatic transfer of phosphoryl groups. And all of the enzymatic reactions involving phosphoryl transfer from ATP (kinases) require divalent metal ions. The one that is usually the natural activator is magnesium. Calcium is sometimes an inhibitor, although it is often a weaker activator. Manganese can always substitute for magnesium. I remember asking Sam Weissman, who is a physical chemist whom I talked to quite a bit, "Sam, what makes magnesium and manganese behave the same?" He said, "They both start with the letter M." [laughter] But the fact is that they aren't so different in size; calcium and magnesium are not only very different in size but their kinetics of complex formation differ by three orders of magnitude. As I mentioned, manganese does activate this class of enzymes, and I knew that manganese was paramagnetic. Did I tell that I had once done some magnetochemistry while I was with du Vigneaud?

GORTLER: No.

COHN: I was always fascinated by it. I had read Pauling's papers on hemoglobin which he published in 1936 (23), where, using static magnetic susceptibility measurements, he had found out what the valence state was of the iron in hemoglobin, methemoglobin, and other hemoglobin derivatives. I thought that was neat.

One of the problems that du Vigneaud tackled was the structure of insulin. It has sulfur amino acids in it, of course. Everything he touched always had sulfur amino acids. The peptides vasopressin and oxytocin that he worked with, for example. I went to him and told him my idea: insulin is crystallized with zinc, but it also crystallizes with cobalt, with nickel, and with cadmium. Cobalt and nickel, of course, are paramagnetic. So I went to him and I said, "I think I have a way of determining what the valence state of cobalt or nickel is in insulin." And he said, "Go to it. Go ahead and do it." So I went up to Columbia, where I knew [Haig Parnag] Iskendarian. He was a physicist, and had been a fellow graduate student. His thesis was on the magnetic properties of D_2O versus H_2O, using static susceptibility measurements with a magnetic balance that he had constructed. He had an exquisitely sensitive instrument for measuring magnetic susceptibility. It was so sensitive that you could only use it after midnight, because it was located in the physics building, which is on 120th Street. The trucks that went by during the day caused enough vibration to make it impossible to use the instrument. I used to start the measurements at midnight. I did the experiments, but I was not successful in evaluating the susceptibility of the metal for the simple reason that the quantity I needed was the difference between two large numbers, the paramagnetic contribution and the diamagnetic contribution. In the protein that diamagnetic contribution is tremendous, so that to decide whether cobalt(II) or cobalt(III) is involved is not easy. The small difference between two big numbers was insufficiently accurate to distinguish if that difference was due to two or three unpaired electrons, and so I gave up. It was not a sensitive enough method to determine the paramagnetism of a metal ion in a protein.

However, when I heard about EPR in the early 1950's, I said, "This is the method," because here diamagnetism makes no contribution, only the paramagnetic species gives a spectrum. By this time I was no longer interested in insulin, but I was interested in the group of enzymes known as kinases, to find the role of the obligatory metal ion in enzyme activity. So that's the reason I started with paramagnetic manganese because it substitutes well for the normal activator, usually diamagnetic magnesium. However, I was very disappointed, because when I added the protein to a manganous chloride solution, the EPR signal disappeared.

GORTLER: Of course, that first experiment was useful because you used it to determine binding constants. [laughter]

COHN: Oh, yes. I made a good thing out of my negative result, but it didn't help me to answer the question about the state of manganese bound to the protein.

GORTLER: In each and every one of your papers, you would mention this fact that the signal disappears, until you finally did reach one paper where you managed to observe the signal in the presence of protein (40).

COHN: Yes. When I learned that Mn-protein had been observed in a solid, I decided one should be able to observe it in solution. It was George Reed, my postdoc, who figured out how to observe it.

Before that, I turned to molybdenum EPR. And that's how I came to publish the paper with Sam Weissman on octocyanomolybdate (24). Because there are a number of enzymes that are molybdenum catalyzed or have molybdenum in them--xanthine oxidase is one. I thought, "Well, I can't get anywhere with manganese proteins. Let's see what happens with molybdenum proteins. But I tried molybdenum chloride first, just to see what molybdenum's spectrum looked like, and I got no signal. I then went to the literature, and found out that Simon Freed (who was, by the way, the mentor of both Sam Weissman and Harry Thode; they both received their Ph.D. degrees with Simon Freed at the University of Chicago) had a paper where he showed that the molybdenum chloride was a dimer and therefore had no paramagnetism. I looked through the literature to find a molybdenum compound which didn't dimerize, and I came across molybdocyanide. I wanted to use it just as a model compound, to see what the molybdenum spectrum looked like.

GORTLER: Right.

COHN: I had to prepare the molybdocyanide myself; it isn't commercially available. So I made it, and I looked at a solution of it in the EPR spectrometer, and sure enough I got a beautiful spectrum. Well, then I started playing with some of these molybdenum proteins, but they were too difficult to work with, they were all light sensitive. At that point I stopped doing EPR temporarily and went to NMR.

GORTLER: You did some experiments with a series of isotopes in the molybdenum paper (24).

COHN: Oh, yes. I didn't do that; Sam Weissman did that. You see, I got this remarkable spectrum of the molybdocyanide. First of all, there are two isotopes of molybdenum, and they were both there, and one could tell what the nuclear spins were. Because of the number of peaks that I observed, one of the Mo isotopes had to have a spin of 7/2. Sam got all excited about this, and he said, "I don't think that's even known. You've just discovered what the nuclear spin is." He went through the literature and found that just that month someone had determined it by another method. I also observed that there was a satellite peak next to every peak in that spectrum. I showed it to Sam, he said, "I don't know what it is." So we went to George Pake. George Pake was in the physics department at Washington University and was the guru of EPR at that time. He wrote a little book on EPR (25). We went to George, and George looked at it and said, "Experimental artifact." So I dropped it. About three or four months later Sam Weissman called me and said, "Mildred, I think I know what those satellite peaks are due to. I think they are due to ^{13}C and ^{15}N. Where did you get that molybdocyanide?" I said, "I made it." I think that's when he first realized that I was a chemist, not just a biochemist. [laughter] It was an inorganic compound, after all. He wanted to know how to make it, and I told him, and he got some ^{13}C-cyanide. He made the compound with ^{13}C and then he got that fantastic EPR spectrum due to the ^{13}C superhyperfine interaction. He wrote it up as a note--a page, I think--in the Journal of Chemical Physics (24), and it is quoted in a book on transition elements by Leslie Orgel (26). He pointed out that it was the first indisputable evidence for electron delocalization in ionic compounds of metals.

[END OF TAPE, SIDE 3]

GORTLER: In 1952 you became an established investigator in the American Heart Association. What did this provide for you?

COHN: It provided my salary completely, and it also gave the institution something like a thousand dollars for expenses.

It was amusing how I happened to get this. I was at a meeting of the American Society of Biological Chemists, and Harland Wood, who was on the research committee of the American Heart Association, told the audience that no biochemists were applying for this grant, and he encouraged people to apply for it. Well, I was very dissatisfied with my salary, which was very low. I was paid less than anyone in the department. Cori was a very subtle man, and so I decided I would approach this subtly. I went to see him and told him that I was thinking of applying for this award. I had thought that if I told him that, he would realize I was dissatisfied with my status. To my surprise, he said, "That's a wonderful idea." I applied for it and I got it. [laughter]

Candidates had to be interviewed by someone chosen by the American Heart Association. I was interviewed by a professor of medicine at the University of Iowa. Before I went I asked Cori if he knew this man. He said he didn't know him personally, but he'd ask the professor of medicine. The latter did know him, and all he could tell me about him was that his father was a classicist, and they used to speak Latin at the dinner table.

GORTLER: [laughter] That's right down your alley.

COHN: The interviewer did ask me why I wanted the award, and I told him one of the reasons was that it was very flexible, that if my husband were to leave Washington University, I could take this with me. He liked that answer.

GORTLER: So, essentially, then you were independent of the Coris, although you continued to work in the same laboratory?

COHN: Well, it didn't really make any difference.

GORTLER: Because you were really independent before that?

COHN: That's right. By that time I had my own grants, you see. In 1946 when I first came there was no NSF and there were no NIH grants.

GORTLER: Then you were dependent on others for salary, but by this time [1952] you were supporting yourself?

COHN: Oh, I didn't pay my salary from my grant. My salary was always paid by Cori. I was independent as far as money for supplies and instruments was concerned. My first grant was $10,000. I was supported by the NSF. Not I, but my research.

GORTLER: You just mentioned that at that particular point you got fed up with EPR, and you turned to NMR. What was your first introduction to NMR and what made it particularly fascinating for you?

COHN: I must have known about NMR in about 1954, because I remember when I got the idea for looking at ^{31}P-NMR of ATP. I was in England on sabbatical in 1955. When you're on sabbatical, you're very relaxed, and you can think about all sorts of things that you're too busy to think about if you're running your own laboratory.

GORTLER: This was Henry's sabbatical, and you had gone with him to England?

COHN: No. We decided to pick a place where we both wanted to go. I inquired from the American Heart Association if they would pay me if I went on sabbatical. And they said no one had requested it before. They were a wonderful outfit. They said, "Sure." So I set that precedent. I was the first one to do that, but other people did it after me. There was no financial problem about my going. We decided to go to Oxford because I wanted to work in [Hans A.] Krebs's laboratory, and Henry thought Oxford would be a congenial place for him. He wanted, in particular, to go to a place where he knew the language, so England was his choice, and Oxford in particular because I wanted to go there and so did he.

GORTLER: I hadn't realized you'd worked in Krebs' laboratory as well.

COHN: Oh, yes, in Hans Krebs's laboratory.

GORTLER: Under another Nobel Prize winner.

COHN: Yes. Oh, yes. [laughter]

GORTLER: Keep the record clean.

COHN: That's right. [laughter] Yes, I worked in his lab. I liked him. He liked me, too. We got on very well, nice man. Too bad he died. All the men I worked with are dead now.

GORTLER: So you decided you could look at ATP and ADP using NMR.

COHN: Oh, yes. You asked me how I first heard about NMR. I heard first about hydrocarbons; that you could tell the difference between, let's say, hexane and heptane.

GORTLER: Right.

COHN: That each of those protons was chemically shifted from the other. I thought that was pretty remarkable. Having gotten that into my head, I started thinking, why not look at the three phosphorus atoms of ATP? One of the things I was interested in, since all of these enzymatic reactions required a divalent metal ion, was which chelate of magnesium was present in ATP? What was magnesium doing in ATP? In fact, this appears in a discussion of a symposium I was at. Al Lehninger asked me a question about it, when I was presenting the manganese EPR results. It's in a book on mechanism of enzyme action from a McCollum-Pratt symposium (27).

In any case, I was very interested in how the magnesium was liganded with ATP; in other words, what was the structure of the the active substrate? Was the magnesium liganded to all the phosphates, or to two and, if so, which two? I thought that in ATP the phosphorus atoms should all be in different chemical environments. If you can distinguish the protons in a hydrocarbon by NMR, these phosphorus atoms should be distinguishable by NMR. The α-phosphorous has a sugar on it, and the -phosphorous is a terminal one, and there's the one in between, which is an anhydride. I decided that I wanted to look at the ^{31}P NMR spectrum.

That was in 1955, when I was on sabbatical. When I came back in 1956 nobody then had a commercial NMR instrument. They had a home-built one in the Chemistry Department at Washington U., but it could only do proton spectra. It was unshielded, and it was so sensitive to external perturbations. The students showed me one day--they had a peak on the oscilloscope, and they took a pair of scissors and opened it, and the peak disappeared. They had changed the magnetic field enough to make the signal disappear.

GORTLER: Was anyone else doing phosphorus at that particular time? I mean, what made you think that you could even do phosphorus?

COHN: Yes, it was known. ^{31}P is a nucleus that has a spin of 1/2 and is 100% natural abundance. It had been done, I don't remember when it was first observed, but not in any biochemical compounds.

GORTLER: Well, it must have been done, because at some point you had to get a probe. I don't suppose you designed the probe.

COHN: No, no. In fact many phosphorus compounds had been done. In fact, Varian had a probe for phosphorus. So I wrote to them in 1956, and they got all excited and they urged me to come on out [to California]. By this time, I had three children. They were all fairly young, and I just couldn't pick up and go out there. I said, "Well, I will one of these days." And then I sort of put it on the back burner.

Two years later, in 1958, my husband was invited to be a visiting professor at Stanford for the summer quarter. I thought, here's my chance to work at Varian. So I wrote to them again in the spring and said, "I'm coming to Palo Alto this summer. I would very much like to look at the proton and ^{31}P-NMR of ATP and ADP and their metal complexes. Can I do it?" They were very stand-offish. In those two years, the organic chemists had discovered NMR and now Varian was selling instruments, and their applications laboratory was very busy showing people what you could do with NMR. I had received such an enthusiastic reception the first time, and the second time they were decidedly cool although they said I could probably manage to get time on the instrument. Well, I was going out there anyhow.

We arrived there in June. The first Sunday we were there, we were invited to the home of a friend of ours, a physicist, and who should be there but Felix Bloch [co-discoverer of NMR]. It was a social occasion, so I didn't say anything. But at one point in the afternoon, Felix Bloch said to me, "And what are you planning to do this summer?" I said, "I was hoping to do some NMR at Varian." He said, "Oh, I'm going out there tomorrow. Would you like to come with me?" Well, you know, it was like being asked by God in the NMR field whether you wanted to go with him. And I said, "Sure." So Bloch himself took me out there. Half of the people at that time who were doing research at Varian on NMR were his former students.

GORTLER: He was a consultant at Varian?

COHN: He was a consultant at Varian. That's why he went out there. He introduced me to the appropriate people, and in spite of that, I was given only two days in the whole summer on the instrument. One of the reasons was that after I looked at the proton NMR of ATP and AMP and ADP, I wanted to look at ^{31}P but they kept the instrument on protons most of the summer.

GORTLER: That must have given a very complex spectrum.

COHN: Not very. The ribose region is very crowded. The adenine only has two protons on it. They're off by themselves, downfield. Actually, Jardetzky published the proton spectrum of the nucleotides in 1960 (28). But I wasn't primarily interested in that. I was interested in the phosphorus. The reason that it took so long to get to phosphorus is that they didn't want to shift from the proton to the phosphorus probe. Finally one day during the summer they did, and they called me and they said I could come and use it. And I did, and there I saw the three peaks of ATP, so I knew the problem was approachable.

GORTLER: And they were splitting one another too.

COHN: Yes, but I don't think I could see the splittings, the resolution was insufficient at that time, though I did see three peaks. I put in magnesium, and I could see the change in chemical shift. Then I put in equimolar manganese, and of course I obliterated the spectrum. By the way, I was using one molar ATP at that time. I don't think anyone had ever made a one molar magnesium ATP solution before. It was decidedly viscous. Anyhow, I found out that I did have a feasible research problem.

When I got back to St. Louis, I talked to my friends in the physics department, and I found out that the University of Illinois in Urbana had just bought an NMR spectrometer. Varian had just then started selling 60 MHz instruments. So I inquired whether I could use the Illinois spectrometer. They finally decided to let me use it on weekends. They had a technician who ran it and I had to pay him. About once a month, I could come up there and use it. That's how it started.

In the meantime, NIH invited Sam Weissman to put in a proposal for an NMR instrument. Sam said to me, "Why don't you come in on this grant?" He asked me to write something up. The idea was that I would have one week a month. I was responsible for twenty-five percent of the proposal. So, after I had been driving myself up to Urbana, and once took the train (that was altogether crazy!) to Illinois...

GORTLER: Do you remember how far it is from St. Louis to Urbana?

COHN: I don't know exactly, I think about 200 miles because it used to take me a good bit of time. I used to do this on weekends, and when I heard we were getting an NMR spectrometer at Washington University I stopped going up there.

When I published the first paper on the NMR of ATP (29), I wanted to acknowledge the use of their instrument. They didn't want me to. They didn't want anyone to know that they had allowed an outsider to use it. So they were never acknowledged. I can acknowledge them now. They were very generous to let me use their heavily used instrument.

Then we got our own instrument at Washington University. It took months to get it to work, because Varian did not have a temperature control on it. They were used to Palo Alto where the temperature is fairly constant. In St. Louis the temperature could drop forty degrees in a day, so it was impossible to run without a temperature control. The chemistry department had given the job of taking care of the instrument to Tom Hughes, with whom I published the paper (29). He was a graduate student in physics who had overstayed his welcome in the physics department. So he accepted this job in order to support himself while he finished up. He was a perfectionist. And he didn't like women either. He was very good technically. When he finally started turning out spectra, they were superb. Nobody else could do it as well. He developed a technique of putting all the power in the side bands, and he really got beautiful spectra. At that time, five millimeter sample tubes were the only ones you could spin. So you could only get a high resolution spectrum on a five millimeter sample. There was no way of averaging, so you were limited to a single scan.

GORTLER: Yes. It was long before either CAT scans or Fourier transforms.

COHN: Yes. That came later. At that time you had to do it in a single scan. To get a high resolution spectrum of the phosphorus of ATP I had to use 0.5 molar solutions. I got an excellent spectrum with all the couplings well resolved, and I did the pH dependence of the chemical shifts of ADP and ATP. That was the first paper (29).

GORTLER: The way you told which one was the γ-phosphorus was by observing the shift of the signal in acid?

COHN: That's right. The β-P of course could be distinguished by the multiplicity of lines. The coupling constants, as it turned out, were the same for α-P and γ-P which was a little surprising. I thought there might be an effect of the adenosine on the coupling constant. But there isn't; the α-β and the β-γ coupling constants are the same except that the α-P is further split by the two protons on the C-5 of the ribose.

GORTLER: They almost should be the same, shouldn't they?

COHN: No. One of them is an ester, and the other one is a phosphate. In other words, that ester moiety doesn't influence the coupling constant. The α and γ shifts overlap at low pH, but as you make the solution alkaline, the γ peak starts moving downfield. In the next paper, I did the magnesium, zinc, and calcium effects on the ^{31}P chemical shift (30), and the effect of Mn^{2+}, Co^{2+} and Cu^{2+} on the ^{31}P line shapes. I also did the proton NMR to see the effect of metal ions. It always bothered me that when you protonate the γ-phosphate, the peak moves upfield, but when you bind magnesium, it moves in the other direction.

GORTLER: The paper with the metals (30); do you think this is your most cited paper?

COHN: Yes. It's a citation classic in Current Contents.

GORTLER: That's obviously fundamental...

COHN: It is used now to determine the magnesium concentration in vivo. From the chemical shift of β-P of ATP one can calculate the degree of saturation with Mg^{2+}.

GORTLER: By the chemical shift?

COHN: Yes, by the shift. The β-P shifts considerably and that has interesting structural implications.

GORTLER: You got a bonus there.

COHN: Well, I didn't use it to determine the magnesium concentration. Someone else did it later, using the shift for that purpose. I first reported this effect, on the question of the effect of metal ions on ATP, in a symposium paper in 1959 (31). You should look at that to see who the discussants were. Everyone from Ron Breslow to [Alexander] Todd. It was a very interesting symposium actually. It was sponsored by the Oak Ridge Laboratory and held in Gatlinburg, Tennessee. About twenty years later, I was at a meeting where three different people showed a figure from that paper! [laughter]

GORTLER: That's rewarding.

COHN: Yes.

GORTLER: In 1958, you were appointed Associate Professor at Washington University. So this was your first line appointment.

COHN: That's right, my first faculty position.

GORTLER: How did that come about?

COHN: When I was first an Established Investigator...

GORTLER: 1952?

COHN: Yes. It was a five year award. When I was first awarded it, the award was renewable. But then the American Heart Association discovered that the people who were their Established Investigators weren't getting tenure appointments because the departments knew they could keep them for ten years on the awards. So the AHA limited the award to five years. I applied for the renewal, not knowing that they had changed the rules. They wrote to me and told me that they really didn't like to renew awards, but since I had no appointment, they would for three years. However, would I ask the chairman of my department what his intentions were. I showed Cori the letter and he said, "Mildred, as soon as there is an opening, you will get it." I informed the American Heart Association; they were satisfied with the response and renewed the award. In 1958, there was a vacant slot, possibly due to Gerty Cori's death, and I was appointed an associate professor.

GORTLER: Could Cori make those decisions on his own? Did he have to go to a committee or some higher authority, or did he have enough clout to get his way?

COHN: Oh, he was one of the triumvirate that ran that school. The three Carls. One was Carl Cori, one was Carl Moore who was the professor of medicine and the other Carl was Carl Moyer, the professor of surgery.

Cori had amazingly good judgment of people. I remember he once interviewed a prospective graduate student, and he then asked me to have a talk with him. Afterwards, he told me exactly what kind of career this fellow would have. And he was right as the next twenty years bore out. This remarkably astute judgment was made when the individual applied to graduate school. I always felt that he would have done well in the Hapsburg court, you know, that fine Italian hand.

Anyhow, Cori kept his word. The next year I was given an appointment. The American Heart Association was wonderful. They had already budgeted for my salary that year, so they gave me the money for research instead, which was very generous of them.

GORTLER: In that second paper, the one where you added the metal ions (30), you comment that you thought that the use of paramagnetic ions would be very promising. It obviously was very promising for you.

COHN: Not only for me. In fact paramagnetic ions are currently used as contrast agents for imaging because they have such a strong effect on the protons of water. They change the relaxation times, the T_1 and the T_2, of water in NMR so tremendously. Those are the parameters they use in MRI [NMR imaging], the T_1 and T_2 of water protons. If the paramagnetic ions are preferentially absorbed and retained as in brain tumors, then you'll get very good contrast in the image.

GORTLER: I see. Now, we'll get to your work there. Essentially you were measuring the effect of paramagnetic ion complexes on the T_1 and T_2 of water protons all through the sixties?

COHN: That's right.

GORTLER: Much the same kind of thing.

COHN: Well, what happened was that I decided that ^{31}P NMR wasn't much use to me because of the very high concentrations you had to use for observation. I did get down to 90 mM ATP for ^{31}P NMR when I used a twelve millimeter tube. Such a tube couldn't be spun at that time, so it yielded low resolution spectra. But even 90 mM is very high for enzymatic work. This was before there were any CATs, computers of average transients. That came later. I decided that ^{31}P NMR of metal chelates of ATP was very interesting chemistry, but for biochemistry at the moment it wasn't very useful. Not that I forgot about it, I figured the instrumentation would get more sensitive as time went on. But it was a waste of time to try to do anything at this point.

GORTLER: Now it's clear as to why there was now this ten-year hiatus. And then you took up ^{31}P NMR again in the 1970s.

COHN: That's right. Now, the one thing that there's plenty of in an enzymatic system is water. So I decided to work with water in the sixties. Since I've always believed, and still do, that one of the most fruitful things is to look at interactions of electron spin and nuclear spin, I decided to use manganese, which I knew would work, instead of magnesium in all these systems. So I started looking at the effect of manganese on the T_1 and T_2 of water with various ligands bound to the manganese. My original naive idea was that I could tell how many water ligands were left on the manganese. I didn't think it would have any other effects. And of course the effect of the manganese is proportional to the number of water molecules in the first coordination sphere of the manganese. In this way, if I bound manganese to ATP and there were three phosphates bound, I could tell the difference between that complex and a complex with two bound phosphates. It turns out that as soon as I started looking at an enzyme complex manganese and ATP, there was a fantastic change in the relaxation times of water. In fact, the relaxation rate increased instead of decreasing. That couldn't be due to the number of waters which could obviously only decrease which would cause an effect in the opposite direction. The effect of Mn(II) on water relaxation should have become smaller, not bigger. I knew, then, that I had a very interesting phenomenon.

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GORTLER: In 1960 you moved to the University of Pennsylvania School of Medicine. All of your early research papers, for about the first ten years, came from the Johnson Research Foundation. What was the distinction?

COHN: It used to be the Johnson Research Foundation/Department of Biophysics. The first time I visited the University of Pennsylvania with my husband--he was being offered the Donner Professorship of Physics--neither the head of the Johnson Foundation nor the head of the biochemistry department was in Philadelphia. They both happened to be out of town at the time. Instead I talked to someone who was the head of the department of biochemistry in the Graduate School of Medicine, who didn't even know the work I had done and certainly knew nothing about me. During our conversation he was trying to place me, and among the questions he asked were did I keep up with things in the field, did I ever go to meetings. I told him that I sort of had to keep up because I was a member of the editorial board of the Journal of Biological Chemistry. I should add that such membership was considered most prestigious; I was the first woman ever appointed, the year was 1958.

Britton Chance, who was the director of the Johnson Foundation, worked in oxidative phosphorylation, an area that I was actively pursuing in the fifties, so he knew me. The Johnson Foundation was far better known for its research than the department of biochemistry. They had no teaching obligations at all, so the concentration was entirely on research. The Foundation had an independent endowment, but it was also the department of biophysics of the medical school.

A week after I got back to St. Louis after that visit to Philadelphia, Chance called me up and asked me to come back. He had returned in the meantime and found out that I'd been here and that we might come to the university. He asked me to give a seminar. It was really amusing--I had such a large audience. They were all so curious about a female scientist. At that time, it was still fairly rare for a woman to give a seminar.

GORTLER: The age of enlightenment hadn't arrived.

COHN: That's right. Anyhow, I came and I gave a seminar. He immediately offered me a job as an associate professor. I talked to Cori about it, because Cori was very wise about these things. I remember when I complained to him when I was going to Harvard for a year about how little they were paying me, he said, "Mildred, the less they pay you, the more independent you can be." I thought, well, if they pay me nothing, I have true independence. The Johnson Foundation had some drawbacks to it that were well known. Cori said, "Why don't you get yourself an appointment in biochemistry too. In case you don't like it, you can move over to biochemistry."

When I came for the next visit, I wanted a joint appointment in the two departments. I went to see the chairman of biochemistry. He knew that I might be coming to Penn, because one of the people in the department, a full professor whom I had known very well in the past, had sent the chairman a telegram concerning the possibility and urged him to offer me a job, which he didn't do. On my second visit I told Dr. [Samuel] Gurin, the biochemistry chairman, that I would like a joint appointment because after all I felt that I was a biochemist more than I was a biophysicist. He said that I could have a joint appointment but I would have to teach, and they couldn't pay me anything. I could have the appointment as a sort of honorary position, but in return for that I would have to teach. So I said, "No, thank you. I think for the first year or two I want to spend time getting my laboratory going." And that was that. Many years later, the school decided that the two departments should merge. So the department became the Department of Biochemistry and Biophysics.

GORTLER: After you came as an associate professor, within a year you were promoted to full professor. Is that another story?

COHN: I must say this for Chance: he's only interested in one thing--whether you produce or not.

GORTLER: I see.

COHN: After a year, he realized that I certainly was as productive as any full professor around, so he just promoted me. There was nothing special about it. Well, it was kind of special because I'd only had a faculty appointment for three years when he made me a full professor.

GORTLER: Right. That's what was a little surprising.

COHN: Well, he doesn't go by the book. First of all, it was ridiculous that it took me twenty-one years to get a faculty appointment, but I must say this for Chance, he shows absolutely no bias--race, religion, sex, it doesn't matter to him. He's only interested in what kind of research you produce.

GORTLER: By that time did you have some very general objectives in terms of the direction in which you were going? You had worked in isotopes early on, then you did work in EPR and then in NMR, much of the time in phosphates.

COHN: Yes. That's a very important aspect of biochemistry, you know, the chemistry of phosphate compounds. The reason that compounds get phosphorylated is to keep them in the cells. Cells take up glucose, but not glucose phosphate compounds. Of course, ATP, adenosine triphosphate, is a central compound in the metabolism of all cells. It functions not only as the reservoir of chemical energy in all cells, but it also has regulatory roles and other roles. It's very important in energy transduction in muscle contraction, bioluminescence and so on.

GORTLER: So basically you wanted to understand the chemistry of ATP?

COHN: That's right. It is a fascinating compound which has so many functions. It's a substrate of the first step in all enzymatic macromolecular synthesis. Whether it's protein, or nucleic acid (where it's actually incorporated) or a phospholipid or whatever, it's always ATP, or in the case of phospholipids, it's CTP [cytosine triphosphate]. In carbohydrate metabolism, i.e., in glycogen formation, the first step involves UTP, uridine triphosphate. It's the triphosphates that are so central to all of the basic bioenergetics of the cell. I've done a little work on nucleic acids, metal binding to t-RNA and NMR of spin-labeled t-RNA (32). But basically, I have been interested in explaining the function and role of ATP in chemical terms in enzyme reactions.

GORTLER: Your first important paper from here was with John [Jack] Leigh (33). This was where you used proton relaxation rates [PRR] for the first time.

COHN: The first paper published from Penn was on metal-ATP, though I did most of the work at Washington University (30). I did a few experiments after I came here.

GORTLER: Right. Yes, but this work with Jack Leigh was all done here. In this paper you look at ternary complexes and you use this new probe (PRR). How did you discover that particular fact?

COHN: I told you that I really wanted to know how manganese was bound to ATP and I wanted to see if I could tell whether there were four or three water molecules left. The manganous aquocation starts out with six water molecules in the first coordination sphere, and I wanted to find out if four or three were left after complexation with ATP. I found out that I couldn't determine that because the relaxation times were neither four-sixths nor three-sixths of Mn^{2+} in water alone. I decided to see if I would observe a bigger change by having the enzyme there as well, e.g., a ternary metal-ATP-enzyme complex. The enzyme might or might not be liganded to the manganese. Lo and behold, I got this fantastic effect when I put in the protein. It was not only very large, it was in the wrong direction. I didn't understand my results at all. I went to a Gordon Conference on Magnetic Resonance where an unprogrammed paper was presented from Bell Labs by the group of Eisinger, Shulman and Blumberg on the relaxation time of water in the presence of manganese bound to nucleic acid and they, too, got this very large change in the wrong direction, when manganese was the ligand to DNA, another macromolecule. I was quite excited about that because I realized that it had something to do with macromolecules. I advised them to publish it in Nature which they did (34). But I was working with proteins. Actually, they had the wrong explanation for the unexpected effect.

It was several years until we figured out the right explanation. The relaxation rate, $1/T_1$, is a function of the dipolar correlation time as well as other variables. The correlation time τ_c can be either the electron spin relaxation time of the paramagnetic ion, τ_s, or the rotational correlation time, τ_r, of the molecule; the observed relaxation may be limited by the rate of chemical exchange between the water in the coordination sphere of the paramagnetic ion and the bulk water. The Bell Lab group had explained the increase of $1/T_1$ on the basis of the increase in the rotational correlation time which certainly does increase in a complex with a macromolecule. The manganese may now be rotating with the same τ_r as the whole molecule. But it turns out that that isn't the explanation for the increased relaxation rate. Whichever τ is shortest is the one that determines the relaxation rate. The electron spin relaxation time also changes when you have the manganese bound to a macromolecule. We actually did a lot of EPR work and determined the electron spin relaxation time in the enzyme-Mn-substrate complexes, and it became clear that τ_s was the relevant relaxation time. In the manganous aquocation, it is the rotational correlation time τ_r which is the predominant contribution to proton relaxation because the electron spin relaxation time τ_s is longer than τ_r and therefore is not the determining factor. It's only when manganese is bound to a protein that the rotational correlation time becomes so long that the electron spin relaxation time is now shorter and consequently modulates the interaction. Never mind what it was due to, I found that I had a parameter with which I could investigate the binding of metal ion and substrates to an enzyme. The reason I pursued it is due to the fact that I had originally expected that this was an NMR parameter that could be measured easily since there's lots of water in the system, in fact 55 molar, so you don't need a sensitive method to study it. Since the magnetic moment of the five unpaired electrons of manganous ion is thousands of times greater than the nuclear magnetic moment of the proton, the effect of very low concentrations of manganese in various complexes could readily be observed. We extended the studies to many enzyme systems and many complexes and the results proved to be quite interesting. One of the important generalizations which resulted from the PRR studies was the finding that as each successive substrate bound to an enzyme, the active site closed up and became progressively less accessible to the bulk water.

GORTLER: I just don't understand how you determine relaxation rates. You're looking at the water protons with the NMR, and...

COHN: Yes. Let me tell you how it's done. The Carr-Purcell-Meiboom technique (35) was the method we used. There are various ways you can do this.

GORTLER: Who built the apparatus to do this?

COHN: Oh, Jack Leigh did that.

GORTLER: Was that terribly difficult? He didn't have to build another instrument?

COHN: There was no pulsed NMR instrument available commercially at the time.

GORTLER: Oh, I see. It wasn't a matter of just attaching something to the NMR.

COHN: No. The reason is that high resolution NMR really is a pain in the neck. The measurement of T_1 of water protons does not require high resolution and can be done very quickly. You can make a measurement of our short T_1s in a minute. I could also do titrations. The measurements required very little volume, fifty microliters was sufficient. I could do a whole titration to determine a binding constant in an hour. If you try to do that in a regular NMR spectrometer it would be time-consuming and require larger volumes.

GORTLER: That's right, you don't have to vary the frequency or the magnetic field.

COHN: That's right and you don't have to shim the magnetic field. Later, in order to figure out the mechanism, we had to do the measurements as a function of frequency and as a function of temperature to find out which τ is determining the relaxation time. The different τ's (τ_r, τ_s, τ_e) have different frequency dependencies. For example, τ_e due to chemical exchange has no frequency dependence and the rotational correlation time τ_r and the electron spin relaxation time τ_s have very different frequency dependencies. Thus, from the frequency dependence you find out the mechanism, that is, which τ is responsible for the relaxation rate. We modified this instrument so that it worked at many frequencies. I have papers which deal with this problem in which the relaxation time was measured as a function of frequency as well as of temperature (36). The temperature dependence, like the frequency dependence, is very different for τ_r, τ_s and τ_e.

GORTLER: So initially, you determined the fact that there was a complex. Then you speculated on the kind of complex you were getting, and, depending on the enzyme, you got different results?

COHN: That's right. Some enzymes bind the manganese directly. In that case we observed a large enhancement of the relaxation rate just by putting the manganese and the enzyme together. Then, when we added a substrate, the relaxation rate went down. With some enzymes, nothing much happened when you just added the metal ion unless ATP was present. Obviously there, the metal was not binding directly to the enzyme.

GORTLER: But finally you were able to determine the number of water molecules that were attached to manganese in the complex.

COHN: Yes, at least the number that were freely exchangeable with bulk water. You had to do a frequency dependence and a temperature dependence study.

GORTLER: In 1963, you received the Garvan Award.

COHN: That's right.

GORTLER: In your Garvan address, you detailed some of the early results (37).

COHN: Yes. That was published in Biochemistry.

GORTLER: Right. Now we jump to 1969 where you published the first paper in which you used two paramagnetic probes (38). That is one in which you used a stable free radical attached to the enzyme; you also used the manganese. Can you tell me a little bit about that work? What prompted you to do that?

COHN: Well, I was looking again at spin-spin interaction. I'd always believed that you could get the most information out of spin-spin interaction, whether it was electron spin-nuclear spin, electron spin-electron spin, or nuclear spin-nuclear spin. And indeed that is, I think, true. It occurred to me that we could find out something about the structure of the ternary complex by having two paramagnetic species in the same complex. Indeed, what we observed was completely unexpected. I expected a change in the EPR line shape, but instead we just got a decrease in the intensity, which was quite amazing. I remember Harden McConnell visited here and I showed him the results and asked him if he could explain them. He couldn't, which made me feel better about the fact that I couldn't explain them. Jack Leigh, who had been my electronics person (he was an electrical engineer by training) came up with a theory.

GORTLER: I assumed that he was your graduate student.

COHN: Yes, he decided to become a Ph.D. student later. The graduate student who was working on the problem, June Taylor, suggested that it had something to do with the magic angle. Jack worked out the theory of showing that the decrease in signal intensity was a function of distance between the two paramagnetic species. It turns out, he tells me now, that the theory was not correct in detail. Other people have since corrected his theory. He had made some assumptions which don't hold. Nevertheless, as a crude first approximation, it was quite useful. It's been referred to as Leigh's theory, because he published the theory in a separate paper (39). It's been used by lots and lots of experimenters to determine distances.

GORTLER: Now he has since gone on to do work on his own in this area. Where is he?

COHN: Oh, yes. Of course. He's a full professor in this department now. [laughter]

GORTLER: I knew that you had commented about consulting with him later on.

COHN: Yes. He's in charge of a project on building an experimental NMR instrument for spectroscopy and imaging the whole body, for humans. The instrument is located in Blockley Hall, in the unused swimming pool in the basement.

GORTLER: I use an office over in Blockley, and somebody told me about their burying this huge magnet.

Before I asked you to do a comparison of Washington and Cornell; now how about a comparison of Penn and Washington?

COHN: Well, as universities go, I must say that I was very disappointed in Penn. When I was at Washington University, I collaborated with a member of the physics department and with two different people in the chemistry department. The departments there are three and a half miles apart, that is, the medical school and the rest of the university. Here where I was just a few blocks away from chemistry and physics, there was no interaction. Washington University fostered that kind of interaction. And this place didn't. One reason, of course, is that this place is so much bigger. I think when a university gets to a certain size, there tends to be more isolation from other departments. There are so many people within your department with whom you can collaborate. At Washington University, there was enthusiasm about this whole business of collaborating with other people. People were always helping one another who were in different departments. For example, I once wanted an enzyme and I knew Paul Berg had been playing with that enzyme. I had no hesitation in calling him although he was in another department--the microbiology department in another building--and I got it from him. In general at Washington University, there was a very good interaction of scientists with one another, even if they weren't in the same department. That's not true here. That's one difference. As far as research went, I had been in a department that was gung ho for research and I was in one here. There were very few graduate students there, and there were very few in the Johnson Research Foundation.

GORTLER: Do you mean the department here couldn't take students?

COHN: No. No, just that the Johnson Foundation had never really been interested in training students. There were plenty of postdocs, you see. There were more than twenty postdocs when I got here. The predominance of postdocs over students was characteristic of every medical school department I had been in except Harvard.

GORTLER: What was the size of the staff in the research center at that time?

COHN: Do you mean principal investigators or faculty?

GORTLER: Faculty.

COHN: When I came there were three besides myself. When we merged, there must have been twenty. That was many years later.

GORTLER: Is that twenty just in biophysics?

COHN: Just in biophysics. Well, maybe I'm exaggerating. There were eight assistant professors, about five or six full professors and a few associate professors, of that order.

GORTLER: And then you merged with the biochemistry department so it was really...

COHN: A very big department then. There was something else I wanted to tell you about the difference though. Oh, yes, about my own position here. At Washington University, I was there for fourteen years, and I never had a student, and I had one postdoc. (That was while I was a research associate, by the way.) Officially, my position was that of a glorified postdoc myself; not really, as I was quite independent at that time. George Drysdale came because he wanted to work with me. But most of the people who came there worked with the Coris. The few graduate students they had, and they <u>were</u> few, worked either with Carl Cori, Gerty Cori, or with one associate professor, Sidney Velick, who was interested in training graduate students. But they didn't have many. They had one graduate student in biophysics when I came here. We decided to try to encourage graduate students, so we formed a committee. I was in charge of recruiting. And we started receiving graduate student applications. Chance would receive many postdoctoral applications, and he urged me to accept some of them. The first two postdocs I had came here specifically to work with me. Many more people applied here than in St. Louis. For the first time in my scientific career I had people working with me. Until 1960, except for a brief period when I had one postdoc, I had worked alone. By the way, after six months that postdoc was put on the faculty as an instructor. He was very good. I didn't have a faculty position, but he did. After all, they couldn't give me a rank as just an instructor, but he was a fresh Ph.D.

I did have Tom Hughes working with me in St. Louis, but he was a graduate student in the physics department. The reason he took the job running the NMR spectrometer is that they told him he could use the instrument to do his thesis, and he did finally get a thesis out of it. Also I had some faculty collaboration as you noted in physics and chemistry. Once I collaborated with Carl Cori, and once with Gerty Cori in the early days at Washington University.

GORTLER: Sam Weissman was in physics or in chemistry?

COHN: Chemistry.

So for the first time I had a group of my own here. The first postdoc was Al Mildvan because he'd read my research papers and wanted to work with me. He had been an undergraduate here and knew the Johnson Foundation. He had worked here as an undergraduate. Then I got into correspondence with someone who was working on creatine kinase from Australia, Bill O'Sullivan. I told him that if he wanted to he could come be a postdoc here, and he did. I had an M.D., Robert Kraus, who was here for a year. He just wanted to learn some biochemistry, and was recommended to come to my lab. Then I had a Japanese scientist, [N.] Itada, who had been working on ^{18}O before he came here and who wanted to work with me. Gradually I got started, and as I got more established, people applied as postdocs. I had some graduate students, too. I'd brought one with me from Washington University with a master's degree from the chemistry department. She hadn't worked with me there, but she wanted to, so she came to Penn. I haven't had many graduate students. In my whole career I've only had six. I've had a lot of postdocs, many of whom were not biochemists before they came, what we used to call 'retread jobs'.

GORTLER: You must have had a certain familiarity with that. You kind of entered the field through the back door too.

COHN: Yes, that's right. I found that generally the people who were chemists adjusted, except one inorganic chemist I had who was quite advanced in years and wanted to shift and that didn't quite work out. I had one physicist who did very well, [B. D.] Nageswara Rao. He's a recent one and was quite an established scientist, an associate professor, before he joined my laboratory.

As you probably know, I had a career investigatorship of the American Heart Association.

GORTLER: Oh. I didn't realize the difference between being an established investigator [1952-1958] and being a career investigator [1964-1978].

COHN: Oh, there's quite a difference.

[END OF TAPE, SIDE 5]

COHN: A career investigatorship of the American Heart Association is a real plum. After I'd been here a couple of years, Chance suggested to me that I apply for an NIH career investigatorship. I said, "No. I don't think so. That's too political. You never know whether they're going to continue it." I said, "What I'd really like to have is a career investigatorship from the American Heart Association." You couldn't apply for that. Their career investigatorship was for life, that is until you were sixty-five. I guess he took it seriously, because in a year I got it; he must have nominated me for it. That was a wonderful award. They don't have it any more, it's too expensive. The American Heart Association paid your full salary. In addition to that, they paid for one postdoc every year and every so often they paid for a senior investigator also whom you could invite to your laboratory. They gave you ten thousand dollars a year to do what you liked with. I always had funds for one postdoc without applying for it, and every once in a while, I could invite a senior person. I did that twice. I had a scientist from Yugoslavia, [Sinisa] Maricic, who was quite an established scientist, and then I had Nageswara Rao from India, who was an associate professor of physics, and an NMR spectrocopist. He decided to stay in this country so that he could pursue biophysics and is now a full professor in the physics department at Indiana-Purdue University. He was very productive and a very good scientist.

GORTLER: Yes. You have a number of papers with him.

COHN: Yes. But he learned the biochemistry, too; I must give him credit for that. I had that support from the American Heart Association until I was sixty-five.

GORTLER: You could also apply for other grants?

COHN: Oh, yes. They didn't care about that. The only restriction they had is that I had to spend seventy-five percent of my time on research. They came and talked to the vice president for medical affairs and to the dean of the medical school to make sure that the administration agreed to these conditions.

GORTLER: Did you do much teaching while you were here?

COHN: No. I didn't do any teaching. The Johnson Foundation didn't teach.

GORTLER: Okay. Then once you had this American Heart Association Career Investigator Award...

COHN: I got that in 1964. So I didn't have to teach all the time I had that. I taught one year after I was 65 and was no longer supported by the AHA. That turned out to be a disaster, but that's another story.

The award gave me a great deal of independence, because I wasn't dependent on the school for my salary and all the extras that I received made my other grant requests smaller. The AHA was an organization that treated you as a gentleman and a scholar. The relationship of that organization to the people they supported was exemplary.

GORTLER: In 1970 you reported on the EPR spectra of protein-bound manganese (II) (40). You really were not able to do that before.

COHN: That's right.

GORTLER: There was a report in the literature that somebody had done this with a powdered solid. You then examined the same compound in solution. Can you tell me something about that, why you were finally successful?

COHN: I didn't realize how anisotropic the spectrum would be in the case of manganese bound to protein. The spectral lines spread over a large range of frequencies compared to the manganous aquocation, over a range where I had never looked. Also one needs much higher concentrations to see the spectrum, because the energy difference of the two states is distributed over so many different transitions. Once I found out that it had been seen, I decided we'd better look for it. I gave the problem to George Reed who has stayed in the EPR field ever since and has done very beautiful work.

GORTLER: Where is he?

COHN: He's now at the University of Wisconsin. But he was a full professor here when he left.

GORTLER: He was a student of yours?

COHN: No, a postdoc of mine. He stayed on, but eventually left. They offered him a very good job out there, and he's very happy. He's a mid-Westerner to begin with. He got his Ph.D. at Wisconsin. He not only did the experimental work, he figured out the theoretical explanation for it. It was, I think, a very important piece of work.

GORTLER: But that was a unique occurrence. You couldn't use that in general.

COHN: You could. Every time I measured proton relaxation rates of water I also looked at the EPR spectrum of the same complex.

GORTLER: But generally you get rather broad peaks.

COHN: It depends on the symmetry of the complex. But at least we knew how to visualize it, even if it was broad. In some spectra the peaks are very sharp but that is, again, a question of the structure. That in itself tells you something. We could always see manganese protein complexes after that because we knew how we had to look over a much broader range of frequency and use a high enough concentration. If you had broad lines or if you had narrow lines, you could always observe a spectrum.

GORTLER: By this time, you're beginning to talk in much broader terms. There's one paper that's titled, "Mapping of Active Sites" and I get the impression that you are much more comfortable with all these techniques that you've been developing over this time (41).

COHN: Well, actually that "Mapping of Active Sites" was due to Jack Leigh's thesis. He really set that all up. This was the paramagnetic effect, not on the relaxation rate of water protons, but on the atoms of the substrate. From that you could calculate distances, since the relaxation rate is inversely proportional to the distance between the paramagnetic center and the observed atom. If you got enough distances you could start constructing a map. Unfortunately, there's something wrong with the detailed conclusions of that particular work. There was an additional complex present under his conditions whose existence wasn't known at the time. There was nothing wrong with his analysis in principle, but in retrospect, it didn't give the right answers. Al Mildvan has been mapping active sites by this method for years. There's a paper by Jack Leigh and Alan McLaughlin and myself where we point out all the pitfalls of the method (42). Nageswara Rao has been doing such mapping more critically and avoiding the pitfalls in recent years.

GORTLER: Where is Mildvan?

COHN: He's a full professor in Johns Hopkins biochemistry department. My postdocs have done very well on the whole.

GORTLER: It appears that way.

COHN: Yes, most of them. Bill O'Sullivan went back to Australia and became chairman of the department of biochemistry at the University of New South Wales.

GORTLER: In 1974 you tackled another new technique. You did at least one paper, you may have done others as well, where you used INDOR and the Nuclear Overhauser Effect [NOE] (43).

COHN: Oh, yes. Now everybody is using it. It's very easy to do with current instruments. It was very difficult to do then. It wasn't easy to measure NOEs. Tom James measured an intermolecular NOE between substrate and enzyme in that paper. Intermolecular NOE had first been done in [Aksel A.] Bothner-By's lab at Carnegie-Mellon, but not with a protein. Our study was the first one with an enzyme. Bothner-By had done it with a ligand interaction between a peptide and a small molecule. Then when Tom James tried to extend it to other proteins after he left here, he told me that it was very difficult. When Nageswara Rao first came, I gave him this problem and he couldn't get anywhere, but the limitation was with instrumentation. Now, everybody does NOEs; that's how they find out what's near what. Our work was done in the prehistoric days but for the same purpose.

GORTLER: Just about that time you could use a CAT to record spectra.

COHN: Oh, no. That came earlier. That came in the sixties. Today it's the pulse techniques that make it easier to measure NOEs, techniques which we didn't have at that time.

GORTLER: Now you press a button and a computer does it.

COHN: Almost. But then it was very difficult.

GORTLER: In a later paper you use ^{31}P again (44). I thought that was a rather cute experiment in which you used a symmetrical reagent which then bound unsymmetrically to the enzyme.

COHN: That always appeals to chemists. In the complex the symmetry of diadenosyl pentaphosphate is broken. That is kind of cute.

GORTLER: That told you what about the enzyme and the inhibitor?

COHN: Oh, it told you how it was bound. That the environment of those phosphates, although they are equivalent in solution, is very different on the enzyme, adenylate kinase. The pentaphosphate with two adenylyl groups is an analog of the two substrates in the reaction of two ADPs to yield an ATP and an AMP. It's a dismutation if you will. The reason that the analog has to be a compound with five phosphates is that if you use one with four phosphates, all anhydride bonds, it isn't long enough to reach between the two binding sites. Nelson Leonard, at Illinois, made the same compound with four phosphates, but he extended the length with two CH_2 groups and the resulting compound worked optimally as an inhibitor. By the way, I didn't discover that, i.e., that the pentaphosphate was a strong inhibitor of this enzyme. My experiment showed that one ADP was in a very different environment than the other ADP.

Nageswara Rao showed later, with the two substrates, that the ADPs were very differently bound to the enzyme (45). One ADP is bound as the magnesium complex, and the other one, no matter how much magnesium you add in the solution, is never complexed with magnesium when bound to the enzyme. The experiment with the substrates and the earlier one with the inhibitor tells you more or less the same thing, they complement one other. Perhaps the most striking contribution of ^{31}P-NMR studies of enzyme-bound substrates to the understanding of enzyme mechanisms was the observation that the value of the equilibrium constant for the central complexes in kinase reactions, that is, $E.S_1.S_2$ $E.P_1.P_2$ is always close to 1 regardless of the value of the equilibrium constant of the overall reaction, that is, $S_1 + S_2 \rightleftharpoons P_1 + P_2$ which in the case of 3-phosphoglycerate kinase is of the order of 10^{-4} (46).

GORTLER: Then you return to your foundations in that you start using isotopes again and you put in the ^{18}O. This gives you a new source of information (47). How did that happen?

COHN: I'll tell you how it happened. I wanted to know whether the protein Tu, an elongation factor in protein synthesis which one of the people in my lab was working with, hydrolyzes GTP to inorganic phosphate and GDP, also catalyzes an oxygen exchange between inorganic phosphate and water. I didn't want to go to the trouble of using a mass spec anymore. I didn't even have one. It occurred to me that ^{17}O was a quadrupole nucleus, and that I could follow exchange with ^{17}O by NMR because ^{17}O would so broaden the ^{31}P of phosphate that its resonance would become invisible. So I made some phosphate with ^{17}O, and added inorganic pyrophatase which I knew catalyzed exchange, and I watched it exchange in the NMR spectrometer. Then I became quite excited because it worked.

GORTLER: You could see the ^{17}O in the NMR.

COHN: No. I was looking at ^{31}P.

GORTLER: Okay.

COHN: If you put ^{17}O on phosphorus, the ^{31}P resonance usually becomes so broad that you don't see it because of its interaction with the quadrupole nucleus, ^{17}O. I figured that as it got hydrolyzed, and ^{16}O was incorporated, the phosphorus signal would rise, and that's exactly what happened. I got so excited, I called my postdocs in; there was [Jacques] Reuben from Israel and George Reed, and I showed them the changing spectra. I said, "Look, this thing works!" The highest ^{17}O I had was only thirteen percent, because ^{17}O was expensive and hard to come by. I happened to have a water sample that was thirteen percent ^{17}O and I made the phosphate by equilibration with water. One of them, I've forgotten whether it was Jacques or George, said, "That line seems to have structure." And the other said, "I wonder if it's an isotope effect?" Then I went and looked at the water I had used. I looked at the label and found it was thirteen percent ^{17}O, but it was about eighty percent ^{18}O. I realized that I probably had an ^{18}O shift effect, so then I dropped the ^{17}O experiment. I made some ^{18}O phosphate without any ^{17}O in it; I used fifty percent ^{18}O so I would see all the species.

GORTLER: So then you could easily distinguish...

COHN: Phosphate containing no ^{18}O, one ^{18}O, two ^{18}O, three ^{18}O, and four ^{18}O. Five species.

GORTLER: Another one of my favorites is the one where you use the ATPβS compound (48).

COHN: I used αS, βS and γS.

GORTLER: Again, it's almost a classical physical organic experiment. Was this something other people were using, because you did write a review article on it a few years later (49)?

COHN: The person who originally synthesized all these thio analogs of ATP was Fritz Eckstein in Germany. Fritz was over here visiting. He had published a paper on this work (50). They had two stereoisomers of ATPβS and two stereoisomers of ATPαS. Obviously the S could be up or down. They had done the NMR on it and they didn't see any difference. When he visited, I said, "Fritz, I don't believe it. There's got to be a difference between one stereoisomer and the other." I thought it was not very good NMR work. I had a student on rotation, and she wanted to do something, so I had her look at these compounds. Lo and behold we got a very nice difference between the two stereoisomers. It just took clean solutions so that you didn't have broad lines. You can't have any paramagnetic impurities in the solution. The differences aren't all that great, but they are different. That's how I got interested in these compounds.

The other reason it interested me; you could buy the AMPS, adenosine phosphorothioate. The first thing I had the student do, before she did the spectral work on the ATPβS isomers, was to do a pH titration of AMP and AMPS. She found a really surprising result. As you titrate from acid to alkaline, for ordinary phosphate the NMR chemical shift is downfield. With AMPS it's the opposite, the shift goes upfield upon alkalinization and the shift is much bigger (51). I have yet to find a theory to explain this. Nevertheless, it was an interesting finding. I realized that the detailed properties of the nucleotides and their thioanalogs were probably fairly different. Why we added the cadmium ion with ATPβS in the hexokinase reaction, I can't remember, but we did, and we reversed the stereospecificity that was observed with magnesium. That's why I did that whole series of experiments.

GORTLER: I liked your explanation, clever and obviously correct, that Mg is binding primarily to oxygen, and the Cd is binding primarily to sulfur.

The last paper you starred for me was a collaborative effort (52).

COHN: Yes.

GORTLER: I know you went to the Fox Chase Center after you became Professor Emeritus here. What is the Fox Chase Center?

COHN: It consists of an institute for cancer research and an oncological hospital. It's had a very outstanding record of research. They have very good people there. They offered me a job a year before I had to retire from the university. I had intended retiring, but at that time my husband was terminally ill, and I knew it, and I didn't want all the structure in my life to disappear simultaneously, so I took the job. I agreed to stay there for three years. At the end of three years they wanted me to continue, but I decided I didn't want to.

GORTLER: So you're no longer there. That's housed where?

COHN: Northeast Philadelphia, the area called Fox Chase.

GORTLER: You published a paper (52) which was a collaboration between the group at Fox Chase and Baylor College of Medicine and Argonne National Laboratories.

COHN: It was my idea. I had become interested in the regulation of kinase activity, in this case, myosin light chain kinase, a reaction involving the transfer of a phosphoryl group from ATP to a serine residue on the protein myosin. The enzyme requires calcium bound to the protein calmodulin, for activation. My object was to study the conformational changes involved in the interaction of calcium calmodulin with a peptide model of the kinase binding domain by high resolution proton NMR. In order to simplify the spectrum of the protein-peptide complex, I wanted perdeuterated calmodulin. I sought out someone who had cloned a gene for calmodulin, Anthony Means and his coworkers at Baylor. I told him what the experiment was that I wanted to do and asked him whether he was willing to collaborate. When he agreed, I called Joe Katz at Argonne. Joe Katz, many years ago, had done a lot of work growing E. coli in D_2O. He told me he wasn't working in that area any more, but Henry Crespi, his colleague in that work was still doing it. I contacted Henry Crespi, who, by the way, I've never met yet, only spoken to him on the telephone, and I told him about the problem and he became excited about it. So that's how it happened.

GORTLER: I see. They all put together the materials and you did the NMR measurements.

COHN: Well, Means' group had to turn over the plasmid to Crespi and he grew the E. coli in the deuterated medium with deuterated substrates, and sent it back to Baylor. They isolated the perdeuterated calmodulin from the bacteria, and then they sent it to us, and we did the measurements. You see there are certain advantages to being established. If I had been just a fresh postdoc with that idea those people probably wouldn't have collaborated with me.

GORTLER: They would have ignored you. That's true. Well, as in so many cases, the more established investigators can handle bigger and bigger problems.

COHN: My collaborators were very pleased with the results of the experiments.

GORTLER: You've been very active in both the American Society of Biological Chemists and the ACS.

COHN: Not so much in ACS.

GORTLER: Well, you did serve once as Chairman of the Division of Biological Chemistry.

COHN: Yes. I was also on the Executive Committee of that group.

GORTLER: I don't know how large the biological chemistry division is in the ACS.

COHN: It's fairly large. But it was very disappointing. We gave out prizes, and when I was chairman, the date of the symposium honoring the prize winners had been changed at the last moment to the first morning of the meeting. We had these really outstanding speakers on the symposium and the audience consisted of the speakers and the members of the executive committee because other people didn't know about the change in schedule. It was just terrible.

GORTLER: I know that well.

COHN: Those speakers weren't used to that. If they had given those talks at an ASBC meeting, there would have been a thousand people in the room for that same symposium. So it was very disappointing.

GORTLER: How did you get involved in the American Society of Biological Chemists? You were the first woman president?

COHN: That's right. I had been elected to the nominating committee and to the Council. Most important, I was the first woman on the editorial board of the journal. One of the main activities of this society is to publish the <u>Journal of Biological Chemistry</u> [JBC]. That's the activity they take more seriously than anything else. In fact I would say it's seventy-five percent of their function. The other function is to hold meetings. I became a member of the editorial board in 1958. That's when John Edsall became editor-in-chief. It was Carl Cori, I'm sure, who suggested me, because the year before he had been trying me out as a referee. I don't know if you know how that journal operates. It doesn't operate like the ACS journals. There's a board of editors and when a paper is submitted, the editor-in-chief decides which member of the editorial board should get the paper. That person decides whether to send it to referees, and chooses the referees. The member of the editorial board is the one who writes the letter to the author after getting referee comments or he may dispense with referees. Then the editor-in-chief signs the letter. The authors don't know who wrote the letter.

GORTLER: As a member of the editorial board, there's actually quite a bit of work to be done.

COHN: That's right. I used to get fifty papers a year. In those days, there were twenty people on the editorial board. Today there are over a hundred.

GORTLER: And they still go through the same process.

COHN: They have added another layer. They have a group of associate editors who cover certain areas, and they're the ones who decide which member of the editorial board the paper should go to. I was asked to be an associate editor, but I turned that down because you have to have a very good secretary or else it's a lot of work. You have to keep track of the papers, when they were sent out, whether they've come back, etc. That's not for me.

GORTLER: At some point in life one doesn't need to do that sort of thing.

COHN: Well, I was on the editorial board for ten years. I paid my dues, as they say.

[END OF TAPE, SIDE 6]

GORTLER: When you became president of the American Society of Biological Chemists, what kind of agenda did you have? Were you concerned with women's issues?

COHN: Not particularly. There were certain issues, of course, that had to be settled. I should tell you how it works. There are two meetings a year of the council convened by the president. There is a list of committees, and the committee reports are considered at the council meetings and recommendations are made. Then, of course, one gets a report from the journal [JBC] and any other issues which may arise. There's one business meeting a year of the general membership, over which the president presides. I apparently had the shortest meeting on record. One of my friends came when it was all over, and he couldn't believe it. He was so used to it going on and on. Some years there have been controversial issues. Occasionally there have been political issues at the general meeting. This didn't happen when I was president, but at other meetings, when certain members wanted resolutions of a political nature to be passed by the group, there was always a hot debate. Sometimes it was rejected, sometimes accepted depending on the issue. At one point... Was it during my presidency? I think so--the question did come up of whether we should meet in a city where the ERA amendment had been defeated. Everything was decided very democratically. There were votes taken on these issues by mail vote if it was so decided at the business meeting.

We had, for example, another issue of whether the executive secretary should be reappointed. That's an important position, because that's the only full-time job and maintains the continuity of the society.

GORTLER: That's a paid position, isn't it?

COHN: Yes. And that became a very pressing issue while I was president. It was the first time in my life that I arranged a telephone conference instead of calling an extra meeting of the council. I'd never done that before. It worked out quite well. Because there were about twelve people on the council, it was quite an undertaking. But the telephone company does most of it for you.

GORTLER: Yes. I would imagine they would. They profit from it.

COHN: I did inaugurate some changes as other presidents before me had, too. One of the big things is the program of the meetings. Paul Berg preceded me by a year or two, and he introduced mini symposia which worked out very well. I don't know when poster sessions were introduced, but they were introduced fairly early and they worked out well, too.

I instituted an organizational change. We used to have council meetings and these endless reports by chairmen of the various committees. I thought that was quite wasteful of time. The council members really didn't have anything to do in between meetings, so I just assigned each one of them to one of the committees as a liaison. I tried to assign the council member to a committee where the chairman of the committee was in the same city. Then if the chairman still wanted to present at the council meeting, okay. Otherwise, the liaison person, who was on the council anyhow would rather succinctly tell us what the committee had been doing, and also the council member advised the committee. I felt there should be more connection between the committees and the council. That I think has continued.

GORTLER: That was a significant change.

COHN: I'm just giving you the flavor of the kinds of things that I dealt with.

GORTLER: Sure. Now they've just changed their name. What is their new name?

COHN: It's now the American Society of Biochemistry and Molecular Biology, ASBMB.

GORTLER: The change took place because it better describes the current activities of the members?

COHN: Partly. The Society wants to attract the molecular biologists as members. First, the Society wanted to attract them to publish in the journal, because some of the most exciting work is in the molecular biology area. They succeeded in that. But they didn't succeed in getting the molecular biologists to come to the annual meeting. The argument was that no one else had included the molecular biologists in any other scientific organization, so they wanted to pre-empt that area and attract these people to meetings. I personally voted against it. I was outvoted, seventy-five to twenty-five, something like that. I felt molecular biology was a subdivision of biochemistry; if someone invents another term, what are you going to do?

GORTLER: Add another term to the name.

You've received a fairly large number of awards at one time or another and been awarded a number of honorary degrees. What in your career has given you the most satisfaction? Obviously an award would probably not be the most satisfying.

COHN: No, the awards came too late except for the awards from the American Heart Association. The first one, the Established Investigatorship assured my salary at a reasonable level for five years as well as my mobility and the second one, the Career Investigatorship not only guaranteed my salary until the age of sixty-five, but also paid for one postdoc every year, for a visiting senior scientist every five years and a $10,000 annual grant to use as I saw fit. This award eased my life greatly--I was less dependent on the university and external grants.

GORTLER: Right.

COHN: As for other awards; after I got the Garvan Award I suggested to the American Chemical Society that they limit it to women under forty, because by the time you're fifty or sixty, it doesn't mean that much to you. They refused. They said there were too many women above the age of forty who should be honored and hadn't been. Well, that means you never can make a change.

What gave me the most satisfaction? Oh, that's hard to say. Let me think. I'll have to think about that a while. I don't want to give you an off-hand answer on that one. Although it is difficult to answer in retrospect (one is never certain that one is not inventing the past), I think the research finding that gave me the greatest personal satisfaction both aesthetically and intellectually was the demonstration of the isotopic shift due to ^{18}O bonded to phosphorus in the ^{31}P NMR spectrum. For one thing, the fact that one could resolve completely resonances which differed from one other by 0.017 parts per million for each ^{18}O was gratifying. From the first observation, I realized its potential in elucidating mechanisms of enzymatic reactions involving the many biologically relevant phosphate compounds and illustrated its value in several different kinds of applications. Finally, it gave me great personal satisfaction because I had, in a way, come full circle. When I was a graduate student, for the first three months that I worked with Professor Urey, I was given the task of calculating equilibrium constants of isotopic reactions from ratios of the partition functions of isotopic species obtained from spectroscopic data. And here I was, more than forty years later, establishing an isotopic effect in particular of ^{18}O in a kind of spectroscopy that hadn't yet been discovered when I was a graduate student.

GORTLER: Okay.

COHN: Of the honors that I've received, probably being elected to the National Academy of Sciences gave me the most satisfaction, because I felt that was a judgment made by my peers.

GORTLER: You concluded your Garvan address on a note of optimism, suggesting that improvements in the techniques and increased sensitivity would allow abandonment of the underhanded methods, that is, things like proton relaxation rates (37)...

COHN: Indirect methods, rather than underhanded.

GORTLER: ...and to look at individual protons and phosphorus atoms in the substrate as it interacts with the enzyme, using what you then referred to as continuous wave NMR. How far have we gotten toward that? We do some of that now.

COHN: My optimism was justified. We've gotten much closer. In fact, even the X-ray crystallographers accept NMR as a complementary technique for structural information of proteins. The sensitivity that was available in 1963 was just so low, I never could have done the experiments that I did in the seventies with the instruments available in the sixties. So I was quite right that we would be able to observe directly the phosphorus and the protons of enzyme-bound substrates. Now, of course, investigators observe protons of the enzymes and obtain structural information. In fact, I underestimated the possibilities in 1963. I never thought it would reach the state that it has. The three great things that have happened, are first of all, Fourier transform spectroscopy--pulsed rather than continuous wave NMR. The second is the availability of higher and more homogenous magnetic fields with superconducting magnets and the last is the introduction of 2-D NMR. As far as sensitivity is concerned, the Fourier transform drastically cut the time of observation and the higher field increases signal intensity and resolution. The 2-D gives you more resolution and other information for assignment of spectral lines. However, 2-D NMR is not more sensitive as far as amount of material needed, in fact it's less sensitive, and you need higher concentrations, actually. There has also been great improvement in probe design which has increased sensitivity.

The magnetic fields have gone higher and higher, but it's questionable whether these very high fields will do as much good with nuclei other than protons, because at high fields the chemical shift anisotropy makes a considerable contribution. The lines start getting broader and you don't get any advantage in resolution. We found that in the ^{19}F NMR of fluorinated t-RNA, that if you went from 100 MHz to 300 MHz you didn't improve the resolution in the spectra, only the quantity needed to obtain them is less. Even though your sensitivity is better and the peaks are spread out, the lines are broader and you're left exactly where you were before as far as resolution is concerned.

There have been such fantastic technical improvements, as well as the ingenious idea of using the Fourier transform. No one could have imagined in 1963 what it would be like in 1989. I remember George Pake, who was originally a student of Purcell, said to me in the late fifties, "It's intrinsically an insensitive method." And that's true. He would never have believed that one could do the kind of experiments that are done routinely now. Of course that was before the days of superconducting magnets of the type we have today. The magnetic fields in commercially available instruments have increased tenfold. They had superconducting magnets, I think, even then, but not any that had the homogeneity needed for the high resolution that we have today. That was a real breakthrough.

GORTLER: Somebody once told me the story that when the physicists saw the first signal, they were pleased just to get one line, that they weren't seeing a difference between protons.

COHN: Well, they wanted to get only one line. They were very upset when they got more than one line. They were only interested in the properties of the naked nucleus. They weren't interested in shifts caused by the chemical environment. That's why, they always used to say, they called it the chemical shift.

GORTLER: Two last, very general questions. One; where do you see the future of biochemistry? From your own experience, where do you see the big fields, the important topics?

COHN: I remember the last time I saw Carl Cori alive, just a few months before he died, about two or three years ago, we were talking about this. He said, and I think he was right, that in his time one was interested in pathways and enzyme mechanisms, and now one is interested in regulation. I think regulation is the really big thing. What regulates all the biological functions in chemical terms? To find out the chemistry of regulation, which is a very broad field. It's a question to be answered whether you're talking about the nervous system, growth and development, or the immune system--regulation of enzyme activity and regulation of gene expression. These areas are being very actively investigated now and where biochemistry will continue in the future. And I suppose structure of macromolecules. NMR still can't analyze the structure of molecules of more than about 10,000 molecular weight, although the limit will undoubtedly be extended in the future. With x-rays now, with the synchroton radiation, one can already look at viruses in molecular detail.

GORTLER: It's absolutely amazing. What advice would you give to a student looking for a career in science today? In particular, a woman student.

COHN: Well, from my own experience and from what I've observed, a woman student should always go into a <u>new</u> area and become expert in that new area. Then when she's ready for a job, there are really so few people who are capable of handling the job, that a woman will be chosen whether they want a woman or not. Also, in a rapidly developing area, there's more opportunity for jobs, for both sexes. But I think for women particularly it's important to go into areas that are newly developing.

GORTLER: Where do you think students should be looking these days? Obviously biochemistry is the hot field.

COHN: Yes. The chemical aspects of molecular biology, cell biology, whatever you want to call it. Cell biology is a very hot field. Immunology is also a very hot field right now, because of the developments of the monoclonal antibodies and the peptide antigens. Structure of macromolecules is essential to understand regulation, for example protein-DNA interactions. I think chemists have much to contribute in all these areas.

GORTLER: Thank you. I appreciate all the time you've spent with me.

COHN: You're welcome.

GORTLER: It's a fascinating interview.

[END OF TAPE, SIDE 7]

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