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Oral History Project

Transcript

David W. Talmage, M.D.
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Williams: This is an interview we're starting now with Dr. David Talmage for The American Association of Immunologists Centennial Oral History Project. Dr. Talmage is a retired distinguished professor of the University of Colorado School of Medicine. He was president of the American Association of Immunologists from 1978 to '79 and served as an AAI Council member from '73 to '78. We're in Dr. Talmage's home in Denver, Colorado. Today is Wednesday, August 29, 2012, and I am Brien Williams.

Dr. Talmage, I'd like to start by your giving me a little bit of your family background.

Talmage: Well, my parents were missionaries, Presbyterian missionaries in Korea, and I was born in Korea. I went to school there through high school, so I graduated from high school in—we had an American school in what is now the capital of North Korea, Pyongyang. I traveled there, stayed in the dormitory, from about the seventh grade on.

Before that, we lived in a smaller town in South Korea called Gwangju, and my folks had a smaller-still home in the country, a little town called Tam Yang. I spent a couple years there, didn't go to school at all. My parents just gave me the books and told me read. [laughs] So when I went to seventh grade in Pyongyang, I knew the vocabulary pretty well, but I'd never heard the words pronounced, so I was somewhat laughed at, made me a little shy.

But I was always interested in science, and even when I was back in the little town of Tamyung, I was always studying astronomy and working out when eclipses occur, the sun eclipse and moon eclipse. I can remember having arguments with my parents about the shape of the eclipse shadow on the Earth. So I've always been interested in that kind of thing, in science particularly and in math.

So then I went to college. I graduated from Davidson College in North Carolina in 1941. I believe it was 1941, just before our entry into the World War II. I went to Washington University in St. Louis on a scholarship. Our parents didn't have any money particularly, and I was given $300 a year for tuition and room and board, and I was able to find a roommate. The two of us lived in the home of a retired minister and took care of his furnace in return for that room. Then I worked on the tables of some of the boardinghouses where the students ate, and I was able to get by, worked my way through college, really, with a very minimal amount of money.

Williams: Let me go back to the Korean era. First of all, what was the nature of your parents' work? What were they doing there?

Talmage: Well, teaching and preaching. My mother and father both spoke very fluent Korean. They went out in 1910, just when the Japanese took over the country,

and at about the same time, and the whole time I was there, the Japanese were running South Korea. It wasn't till the end of World War II that the Japanese had to leave. So from 1910 to about 1945, Korea was under the rule of the Japanese government.

Williams: How did that Japanese control affect your parents' work, if at all?

Talmage: Not really very much. Toward the end, the Japanese became very dictatorial and insisted that everybody bow and make obeisance to the Japanese emperor. When Pearl Harbor was bombed in 1941, December the 7th, I was in medical school in St. Louis, Washington University. At that time, the Japanese demanded from my father that he sign over all the mission property to the Japanese government, because the war had started. After Pearl Harbor we were at war with Japan. Since my father refused to do it, he spent four months in jail, a local Japanese jail. He's written a book about his experiences during those four months. In the end, they had him on rice water for a couple of weeks.

But suddenly some negotiation between the Japanese and Americans for a swap of prisoners, and they were fortunate to be able to come home then, so although they had a very hard time for four months, after that they were able to get on a ship and go to South Africa, where the prisoners were exchanged. They got on another boat, went back to U.S.A., and they spent the rest of the war in this country.

Williams: In Georgia?

Talmage: Well, yes, it was in Decatur, Georgia, that's right. That's where we lived. Of course, by that time I was in medical school and graduated in '44. Normally, the medical school curriculum is four years, but during the war they shortened it to three years by making us go to school all summer. I graduated in '44 and then took one nine-month internship in Atlanta, Georgia, so we had some connection with that state.

Williams: You have siblings.

Talmage: Right. I was the sixth of seven children, so I had four older brothers and one older sister and one younger sister.

Williams: Did any of them become scientists?

Talmage: Yes. My brother who's just older than me, a couple of years, was a biologist. He ended up he was first in Texas at Baylor [University], and then he moved to North Carolina. He ended up he was professor of orthopedics because his research was in bone, calcium. So that's the only sibling who was interested in science. Both my sisters were nurses at one time.

Williams: What about your other brothers?

Talmage: My oldest brother was an electrical engineer. He worked for RCA when they were developing television, and he was involved with that to some extent, I think. Then the other two brothers were ministers, Presbyterian ministers.

Williams: That leads me to my next question, and that is how important has religion been for you?

Talmage: Well, I think it's been very important in terms of the development of values. I have been a moderately active member of our church. I've been on what the Presbyterian Church has, what they call a session, which is the ruling body of the church. I've been on that, and so I've been somewhat active, but I've never been very dogmatic about religious things. I've always had an open mind, and I'm sure some of the scientific things that I came up with would have shocked my parents, had they really understood what they were. [laughs] But I was open to whatever I found, you know. Religion, I always had it as a good value and a good thing for society, but I've personally never been a very dogmatic religious person.

Williams: Have there been times when your science and your religion have been in conflict?

Talmage: Well, they could have been, but they never bothered me. I was, first of all, a scientist, I think. So the religion never kept me from finding out what was true and, in a way, religion maybe helps you in that it teaches you that there is a reality. I've always been interested in what really happens.

Williams: You write in your autobiography that your father encouraged you, or maybe insisted, that you go first to Maryville College, because he did think he wanted to steer you into a religious life.

Talmage: Right. I think that's probably true.

Williams: Then how did it come about that you transferred to Davidson?

Talmage: Well, I don't remember exactly, but I had this friend who was a neighbor in Korea with the Wilson family. Dr. Wilson and his family, they had seven children just like we did, and they lived right next door to us. He was a very nice guy, and I was very impressed, you might say, and stimulated by his work with the lepers. He directed a leper colony there, and at that time in Korea, the lepers were not treated. They were just turned out and they roamed the streets. Everybody stayed away from them. He founded this leper colony, and it was, to me, a very impressive thing to do.

Williams: So when you got to Washington University, were you already engaged in the whole notion of immunology?

Talmage: No. When I went to medical school, I had an interesting roommate. Alexander Ling turned out to be my roommate when I got there, and he had applied, had been accepted at Stanford [University] Medical School, but his acceptance of the acceptance never reached Stanford, so they assumed he was lost and they replaced him with somebody else. So when he got to this country, went to Stanford, he found out they didn't have a place for him. But they got on the telephone and arranged a spot for him at Washington University, and he ended up as my roommate. I can remember neither of us had any money, and we'd cook rice in our dormitory room over a hotplate. [laughs] That's how we got along, and it was wonderful.

Williams: So when you left Washington University, you were where in terms of your science career?

Talmage: Well, in medical school I was always interested in the basic science behind the studies that we did, and I would have, if I had an opportunity, done research in medical school. But because of the war, three months after I got there, Pearl Harbor was bombed, and we were all inducted into the Army, and I spent the rest of my medical school as a private in the Army, and we really didn't have much time to do research. So I didn't really get into research until I got back from my Army service in '48. I graduated from medical school in '44, and then I was in the Army for three years, I think.

Williams: Curiously, you were stationed back in Korea.

Talmage: Well, the way that happened, I was sent to the Philippines, and when I got down there, they had more doctors in the Army than they needed. So I didn't have much to do, and I heard there was a cholera epidemic in Korea because of the returning refugees that came back to Korea after the war ended. I went to my commanding officer and told him I spoke fluent Korean, which was a little exaggeration, because it had been a while. But, anyway, they arranged a transfer to the military government, and I went to Korea and served as an advisor to the new Korean government as part of the military government.

Williams: Were you at all surprised in '51 when the North Koreans invaded?

Talmage: Yes. Fortunately, I wasn't there. [laughs]

Williams: I know you weren't, but, I mean, did you see unrest when you were there?

Talmage: No, that was a total surprise. There was no reason for that, as far as I know, other than that they had a big Army, and they wanted to take control of the whole peninsula. I guess there was just too much for [Harry S.] Truman, and he told [Dwight D.] Eisenhower to defend the Koreans, so that's how the Korean War started.

Williams: Right. So you had a fellowship then at Washington U.

Talmage: Right.

Williams: And you worked there with Frank Dixon.

Talmage: Right. That's right.

Williams: Talk about that connection.

Talmage: Well, when I came back, I had an appointment as an intern at Barnes Hospital. I had served as a rotating internship before I went to Korea, and then when I came back, I had a straight medical internship at Barnes Hospital. Then after that, I had a job with Frank Dixon, and we did research on radioisotopes, which were new at that time. They had been developed at Oak Ridge [National Laboratory], and we used to get the radioactive iodine on a weekly basis almost from Oak Ridge. Iodine has a half-life of about eight days, and we would have to get a resupply fairly often.

We attached the iodine to protein antigens. Usually the one we used the most is bovine gammaglobulin, and we used to inject them into rabbits and then bleed the rabbits. We discovered that you could tell when the antibody response occurred, because then the antigen would rapidly disappear from the blood, because the antibody would agglutinate with it and would be absorbed by macrophages in cells like that.

Williams: So this launched you on the path to immunology.

Talmage: To immunology, right. That's how I got started in immunology.

Williams: And Frank Dixon was critical in that. Is that correct?

Talmage: Right, yes. I learned a lot about how to do research and write papers and research grants.

Williams: Then you went with him to Pittsburgh.

Talmage: Right. I spent a year with him in Pittsburgh. He was professor and head of the Department of Pathology there. We had a great time there.

Williams: Was your research kind of a continuation of what you'd been doing at Washington?

Talmage: Yes, it was. It was really a research into the study of antibodies. At that point, immunology had reached a stage where it was possible to isolate the gammaglobulins, and we knew that the antibodies were in the gammaglobulins,

and it was possible to study antibodies serologically. So I would say that's a phase of immunology that we could call serological phase.

We learned about the effect of radiation. Well, that's the main thing Dixon was studying then, the effect of radiation on the production of antibodies. It was very interesting, because if you irradiated an animal before you injected them with an antigenic stimulus, if you irradiated them first, then they wouldn't respond to the antigen. But if you gave them the antigen for a day first and gave it a chance for things to start, you could irradiate and they'd still make antibodies.

So something was different about at some stage of the process was radiosensitive and other stages were not. So that was how we got interested into that, and then I carried that on when I went to Chicago and I worked with a man named Taliaferro. Dr. Taliaferro was spelled Taliaferro, but we pronounced it "Toliver." He and I had a close relationship. I had lunch with him once a week, and he was very allergic to animal dander, so he couldn't work. [laughs] He couldn't work in the laboratory, but his wife was an excellent technician, and she did all the experiments that we designed. So that was very good. I learned a lot from that.

Williams: Was that a continuation of the radiation work?

Talmage: Yes. Dr. Taliaferro was also interested in radiation, effect of radiation on things, and he knew a lot about the histology of lymphocytes and lymph nodes and the lymphatic system, which was the obvious source of antibodies. Because one of the things that Dixon had done was he showed that if you immunized an animal and after they have an immune response, you take out the lymph nodes or the spleen and you inject the lymphocytes into another animal, you transfer the ability to make antibody with [those lymphocytes]. So we knew that the lymphocytes were the source of the antibodies somehow. So that's, I'd say, when we went from a serological phase of immunology to a cellular phase. About that time, I'd say cellular immunology became very important.

Williams: What is the importance of that difference?

Talmage: Well, it's just a more basic understanding. We didn't discard what we knew about the serology, but we were going down to a more basic so where's the source of this antibody that's in the serum. Where'd it come from? There was a lot of study around the world. There was a demonstration of what are called plasma cells, and the plasma cells made gammaglobulin.

There was a disease called multiple myeloma. I don't know if you've heard of that. That's a disease of the bone marrow, primarily. It's clear that the extra gammaglobulin that these cells make are derived from plasma cells. So, gradually we began to learn more and more about the cellular source of antibodies. That's when the idea of cellular diversity came in, the fact that different cells made different antibodies.

Williams: You mainly did that work while you were in Chicago?

Talmage: In Chicago, right. There was a Danish immunologist named Jerne, Niels Jerne. He had published a paper on antibody production, and he had a theory, what you call natural selection theory. His idea was that somehow the plasma cells or the lymphocytes of some cell could take in the antibody that was attached to the antigen and make more copies of it. He hadn't gotten to the stage where he thought that the cells were diverse. He knew that the serum was diverse, but he didn't go to the stage of having diverse…so it shows how things go step-wise.

Williams: What lured you to Colorado?

Talmage: Well, we lived in Chicago for seven years, which were good years. We had difficulty finding a place we could live near the university, which is South Chicago. I don't know if you're familiar with where it is. The university has a fine campus there, but the surrounding area did not have the kind of housing that we needed.

So we found a place that we could use out in La Grange, which is a suburb of Chicago. It took about forty-five minutes to an hour to drive in. I had a good friend there named Mark Dean [phonetic], and he and I would drive in together. We had wonderful conversations about these kinds of things at the time, I remember, very important.

Williams: So you got tired of that drive and decided to move to Colorado.

Talmage: That's right. [laughs] Well, and the weather here is much better. We have wonderful weather here. I mean, look what it's like today, and although it's going to be ninety, it cools off at nighttime and it's not that uncomfortable in the house right now, because we've cooled it off during the night.

Williams: Right. So it was these sort of personal things that—

Talmage: That had an effect, and also I was offered a nice job.

Williams: They sought you out?

Talmage: Right. Actually, we were down in Pasadena at Caltech [California Institute of Technology]. I was on a three-month—I believe it was a three-month sabbatical and working with an immunologist named Dan Campbell. I don't know whether you've run into him or not, but he was a very interesting, likable guy, but he didn't care for cellular approach to immunology. He was strictly a serologist. He just hadn't been able to make that next step.

So, anyway, we had a great time down there, and while I was there I was invited to Denver to look at a position here at the medical school in preventive medicine, and I came and looked at it. It obviously didn't fit, because I was an immunologist. There's some relationship between immunology and preventive medicine because you immunize people to prevent disease, but it didn't seem to fit.

So a few months later, I was invited back to look at the allergy job here, so I came and it seemed like there were no immunologists in Denver, and I would have an opportunity to do research. So we liked it and my wife liked it and children have liked it, have become great Bronco fans. [laughs]

Williams: So what was it you built then, a program would that be true to say?

Talmage: That's right, yes, and a number of fellows. One of them is Henry Claman that we can talk about a little bit more. But I had, I would guess, a dozen different fellows working in the laboratory. It was a very exciting time because it was just the idea of cellular diversity and cellular selection hadn't been quite accepted generally, but it was in the process. It was the time when immunology went from being a purely cellular discipline, from cellular we went to genetic, so we went another step more basic into the genetic basis, and a great deal was being done in cellular biology with new techniques of studying DNA.

You know, in 1953 was when the discovery of the structure of DNA by [James D.] Watson and [Francis] Crick. That was right then in that time, and, of course, the development in the related areas adjoining immunology are very important, and the ability to study DNA was just becoming, and it was during that time that it was discovered that the DNA had a code for the translation into protein. That was all very exciting, and soon it became possible to isolate the genes that make the antibody, and we discovered there was a constant region and a variable region, and that there were many different variable genes, but only a few for the concept. The whole genetic structure of antibodies was developed during those few years, and that was very exciting. When I first came to Denver, that's when all that was taking place.

Williams: Were you the hotbed center of that activity, or was it going on pretty universally?

Talmage: It was going on a lot of places, particularly in Australia, and it was going on in quite a few different places. But I think we were right up there. This is where Henry Claman came in, because he worked on the thymus, and he was the one, I think, that discovered that the thymus cells and the bone marrow cells cooperated to make antibody. He called the bone marrow cells the B cells and the thymus cells were the T cells. He found out that if you just injected one, you didn't get much antibody, and if you injected the both of them, you'd get a lot more antibody. So that was a very major discovery.

Then the Australian discovered that the B cells were the cells that actually made the antibody, but the T cells were the helper cells, and they made some kind of juice. They made a substance that stimulated the B cells to make the antibody. So it was very exciting all this was uncovering. At the same time, people were learning about the ribosomes and the genetic code and all that was coming out.

Williams: Was Claman the one that first called them B and T cells?

Talmage: Yes.

Williams: And he was working with you?

Talmage: Yes, he was in my laboratory. He's still here. I think he never got full credit for all that. A lot of these things, you know, happen rapidly, and it's hard to sometimes know just who to give credit for. Anyway, he didn't stay in that kind of work. He got off into studying the effect of cortisone and other things and more clinical immunology, and I think he lost contact with what more basic things were happening. He's still a very active immunologist, though he's retired.

Williams: Now, your own career was taking a little bit of a different tack, because then you got into administration.

Talmage: Right. It happened at that time while I was running the allergy laboratory that they needed someone to chair the Department of Microbiology and Immunology. So at that time, microbiology and immunology were in one department, and they offered me that job, and for about three years I was the chairman of the department.

Then at the end of that time, the reason I got out of that is that the chancellor needed somebody to help in the administration of the medical school. John Conger was both a chancellor of the medical center and dean of the medical school, and so I went down there first as associate dean and then finally he separated the jobs and I became dean of the medical school for a couple of years. I always said that it was such a nice job, I wanted to share it with other people, because when I had an opportunity, I got out of it. I really was interested in the research.

Williams: These positions took you somewhat or maybe a lot away from research?

Talmage: Well, not completely. I maintained my research laboratory, and I had a good couple of assistants there who worked in the lab. I had a research grant all that time, and we made a few interesting studies.

Williams: Without getting into a lot of details, the main focus of your work then was what during that period?

Talmage: Well, we were interested in a phenomenon called antigenic competition, and we wrote several interesting papers about that. We were also interested in the way to identify antibody-forming cells in an agar dish plate. You could count how many antibody-forming cells there were on a plate, because each cell made enough antibody to lyse the red cells in that agar, and you could see a little clear spot where the antibody-forming cell was. That was an interesting technology that developed and advanced the cellular portion of immunology.

Williams: You left the deanship in '71, but three years later you took over the directorship of Webb-Waring [Institute].

Talmage: Right.

Williams: So how come?

Talmage: Well, there was an opportunity to really have a research laboratory with a lot of assistants, and we were able to expand. One of the people that I brought to there for a while was Kevin Lafferty from Australia, and I had gotten to know him before because we had taken a sort of a vacation or sabbatical in Australia. I had worked in his laboratory, and he came back and worked at the Webb-Waring for a few years.

Then eventually he became director of immunology at the Barbara Davis Center for Diabetes, and there was a great deal of effort to understand how we could transplant the cells that make insulin. So there was a strain of mice called NOD mice. The strain of mice developed diabetes spontaneously, and so it was a wonderful opportunity to do experiments, transferring antibody-forming cells and seeing if you could transfer insulin-producing cells and see if they could cure the diabetes.

Williams: Unfortunately, that didn't happen.

Talmage: Well, it did in mice. [laughs]

Williams: Good news for them.

Talmage: That work is still going on, attempts to recognize which children are likely to get diabetes and ways of testing and determining who has the greatest probability of getting diabetes and preparing. So there's a lot of work going on in that area, and I don't know just exactly what stage that is in right now.

Williams: I read with interest your 1977 article on your goals for the Webb-Waring, and you had five, I believe, and two of them intrigued me particularly. One was you wanted to increase the interdisciplinary research.

Talmage: Right.

Williams: The other was create a bridge between basic and clinical services. I'm wondering, did you succeed in those two goals?

Talmage: I think somewhat. I wouldn't claim that we were totally successful, but we made progress. I recruited a gentleman named John Repine, who's a young man from Minnesota who was interested in oxygen toxicity. We had been working with oxygen toxicity to antibody cells, and Kevin Lafferty, who had been in the Webb-Waring, had worked out a way that if you expose the transplant, use the model of a thyroid transplant, and he was able to transplant thyroid glands from one mouse to another by putting the thyroid underneath the capsule of the kidney, and then you could find it. Then he was able to transfer islet cells from the pancreas, which are the cells that make insulin. He was able to do that and learned a lot about that, but, unfortunately, none of that has been completely applicable to humans. So I think we made a lot of progress in the basic work, but the transfer of that knowledge to human use has been much slower.

Williams: In 1988, my notes say you retired.

Talmage: Right.

Williams: How come?

Talmage: Well, I was sixty-nine years old, I guess, and I felt that I was having a harder time getting grants, and it was time to turn it over to younger people.

Williams: Did you maintain any presence at the Webb-Waring?

Talmage: I didn't at first. For several years I got out of the way entirely from Webb-Waring. They had a director called Tom Petty, and he ran the place for a while, but then he retired or left the Webb-Waring, and I served as an interim director again for a couple of years till we recruited John Repine, who's been there for twenty-five, thirty years since '88, anyway.

Williams: In 1954 you became a member of the American Association of Immunologists.

Talmage: Yes, that sounds about right.

Williams: What motivated you to do that?

Talmage: I was in Chicago and I was becoming an independent researcher. I left Dixon's group and went to Chicago, so it was a natural kind of thing to do. I'd been going to the immunology meetings every year. We used to have one every year in Atlantic City, and it was a great occasion. So naturally I wanted to be a member of the organization.

Williams: Was that sentiment fairly universally shared?

Talmage: Yes. I think immunology was a growing specialty.

Williams: So, actually, the organization is kind of a recognition of that growing.

Talmage: Yes.

Williams: Then you became involved in the editorial activities related to the journal.

Talmage: *The Journal of Immunology*, I never was on the editorial.

Williams: Really? I think you were on the editorial board.

Talmage: I was the editor of the *Journal of Allergy*.

Williams: Right.

Talmage: But I don't think I was ever—

Williams: You were never the editor.

Talmage: I never was the editor.

Williams: But you were associate editor.

Talmage: I may have been on the editorial board.

Williams: Right. You were. Then in '73, you began what I called a kind of path or stream that leads to the presidency through the council.

Talmage: Right. I got on the council.

Williams: What motivated you to do that?

Talmage: Well, I don't know. It just seemed like a good thing to do. [laughs] I was interested in immunology and in the organization, so it was a natural thing to do. You know, you don't nominate yourself for that kind of thing. You're asked if you'd like to run, and usually they have an election of three or four people each year, and one of them gets elected to the board and then after a few years they become candidates for president. That's how that happens.

Williams: You won in your first go-round?

Talmage: I think so, yes. [laughs] That's over fifty years ago.

Williams: Then you served as president from ’78 to ’79.

Talmage: Right.

Williams: What was that like?

Talmage: Well, it’s not a very arduous task. The main thing is you get to give a presidential address at the annual meeting, and that’s one thing I was able to do. I can remember that.

Williams: Seventy-eight, ’79, that was the last years of [James E.] Jimmy Carter as president. Was there any responsibility you had as president, in terms of promoting the interests of the field on the political scene?

Talmage: Not politically, but I was on the National Institutes of Health Council for the Immunology Institute. So I served for many years on that council, which in the last analysis determined who got the grants. But, of course, every grant went through a process of being scored by a committee and generally we stuck to the scores, and the high scores got the grants. But the council had the authority, if they felt, to raise somebody’s score if they felt that was a very important area.

Williams: Did you do very much of that?

Talmage: No. I mean, we discussed it occasionally, but it was very limited. I think the council’s careful to not overstep their powers.

Williams: What was federal funding like for research in those days?

Talmage: It was much easier than it is now, I can tell you that. Well, what’s happened, I guess, is the number of scientists has expanded and the amount of money available has decreased, so it’s become a tighter and tighter competition to get a grant.

Williams: But in your time, it was sort of the heyday of—

Talmage: Yes. I was able, without difficulty, to get a grant every year, so no problem. That was a time of expanding science.

Williams: Now, I noticed you also, from’81 to ’83, served as the representative for AAI at FASEB’s [Federation of American Societies for Experimental Biology] Public Affairs Committee.

Talmage: Right.

Williams: Now, that would have been the first two years of Ronald Reagan and government cutbacks in spending and whatnot.

Talmage: Right.

Williams: Was that an issue that you dealt with with FASEB?

Talmage: It was always a problem with trying to maintain as much support as we could. Everybody's after that federal dollar. So it was at the NIH, and, of course, the money had to be divided up between the various institutes. That was, of course, a matter. But the FASEB didn't have much power, actually, you know. I think they were, you might say, a customer. The FASEB represented the scientists and did what they could politically, but they didn't have any direct power over what happened. It was up to the politicians.

Williams: So FASEB didn't have lobbyists on staff or on hire and things of that sort?

Talmage: I don't think so. I know we were asked to go and testify, and I did that once or twice, but nothing much happened of it, other than you would go and give a little talk and say how important research was to the advancement of knowledge, that sort of thing.

Williams: Were those memorable experiences for you?

Talmage: Not particularly. I wasn't that impressed. [laughs]

Williams: Now, you took the opportunity in your presidential address in '79 of doing something that probably not too many other presidents had done, which was sort of review the history of the organization.

Talmage: Right.

Williams: What led you to do that?

Talmage: Well, I was interested in it because Dr. [Gerald Bertram] Webb, who founded the Webb-Waring Institute in Colorado Springs, he was a doctor working in Colorado Springs, and he had his own little animal laboratory back behind his house. He worked on tuberculosis, and he discovered the relationship between lymphocytes and tubercular immunity. He didn't know anything about what came about later, but he was an important step to know that the lymphatics were involved in immunity. He noticed there is some relationship between altitude and tuberculosis and people would come out and live in the mountains in the clean air and it was helpful in their recovery from the disease.

But he actually was important in founding the American Association of Immunology. The word "immunology" itself was a new word, and someone had suggested other words, but he suggested that we call ourselves immunologists. He was, I think, one of the first presidents of the organization, if I'm not

mistaken. That was about—well, we know it's a hundred years, so that was in 1913.

Williams: Then in '88 you wrote another paper on the occasion of the seventy-fifth anniversary of the American Association of Immunology.

Talmage: And I reviewed the history again.

Williams: Right. In that you said that cell immunology was still a newer development.

Talmage: Right.

Williams: I'm wondering has anything succeeded that, gone beyond that, or is it still at that stage?

Talmage: I think I hinted in that paper that we were going into the genetics, the study of genetics. At that time they were beginning to find genetically altered mice. They could grow mice as purebreed, and they were able to get mice that had particular deficiencies in their genes, and that way it was one way of studying the scientific basis of immuno-production immunology.

So we were getting into the genetic, and then I could see that from genetic we were getting back to the whole animal. So it was a full circle. The immunologists started out as a study of animals or human beings, the whole animal. That's how immunology began with [Edward] Jenner and [Louis] Pasteur and so forth. So we go from the animal to the serological, to the cellular, to the genetic, and then we were getting back into the animal who was deficient genetically. So I could see there was a certain circular to it, and maybe this was a good thing. I don't know. I thought it was.

Williams: Did the molecular level play a role here?

Talmage: Molecular immunology, sure. Maybe you would say the genetic was part of the molecular.

Williams: Is that pretty much where we are today?

Talmage: No. I think we've gotten back into the study of the animal.

Williams: We're about to celebrate the hundredth anniversary of the American Association of Immunologists].

Talmage: Right.

Williams: I'm wondering what you might have to say to your colleagues who will be assembling for hundredth anniversary about the field and your lifetime experience in it and so forth.

Talmage: Well, all I can say is it's been a wonderful, wonderful career and very exciting area to study. I think we've made a lot of progress in not only immunology, but in biology as a whole with the discovery of the importance of DNA, the genetic code, and genetic diseases, and all that has been a revolution, you might say. I always say it began with Dr. Jenner, who did the first cowpox vaccination in about—I think it was 1797, somewhere around there. That experiment was probably the most useful, in terms of saving lives, of any experiment ever done by human beings. But it would not pass our research committees today, because what he did was he gave smallpox to an eight-year-old boy. It would be forbidden today to do that. I don't know whether he got the parents' permission, but probably he got the parents' permission.

At that time, smallpox had about a 50 percent mortality if you got smallpox, but there were strains of smallpox which were much lower mortality, and people were using that as a way of immunizing people against the deadly disease. Then Jenner discovered that the girls that milked the cows would get pox sores on their fingers and they'd never get smallpox. They were the most beautiful girls there were, because everybody else was pocked, but these girls never got smallpox.

So he got the idea, "Well, why don't we use the cowpox to immunize instead of this less virulent smallpox?" The smallpox vaccinations, there was about a 2 percent mortality, and by using the cowpox, he got rid of the mortality altogether except in very occasional immune-deficient individuals. That was kind of interesting.

When we came to Denver, the head of pediatrics was Dr. [C.] Henry Kempe, and he was interested in smallpox. He and Dr. [Gordon] Meiklejohn, who was chairman of medicine, together they worked on the worldwide eradication of smallpox. So that's a very interesting subject in itself, the history, and that's, I think, where modern medical science began.

Then after Jenner came Pasteur. Then it was Koch in Germany. In about 1850, the microscope was developed so that you could actually see bacteria under the microscope, and between 1880 and 1890 there were ten diseases identified as caused by bacteria.

Williams: It was a very productive period.

Talmage: It was a very productive period. Then, of course, you know, around the turn of the century, it was [Karl] Landsteiner and the discovery of the blood types and the ability to transfuse people with compatible blood types. There was the discovery of the importance of the mosquito in viruses, yellow fever, and malaria. The

building of the Panama Canal, all of that history developed around the early 1900s. So biological sciences have really been revolutionized in the last hundred years.

Williams: Do you ever question your decision to go into that field?

Talmage: No, not at all. It's been a very rewarding experience for me. I treasure the memories.

Williams: What do you consider your legacy?

Talmage: I think the most important work I did was in developing the idea of what is called cell selection, where the idea is that different lymphocytes make a different gammaglobulin and that what the antigen does is selectively multiplies the cell that makes the globulin that serves as an antibody, that all antibodies are natural globulins. The body makes the globulin already, and the particular cell that makes that globulin, it has a cell that makes a globulin that serves as an antibody to measles. But when you're having an attack of measles, those cells multiply maybe a millionfold, so the next time you're exposed to the virus, you don't get the disease. You just get measles once. That's how the immunity works. That idea, I think I can take credit for that to some extent.

Williams: What accounts for the huge growth in that particular lymphocyte?

Talmage: Well, that's where the cellular immunology comes in, you know, and the T cells and the B cells.

Williams: What triggers that productivity?

Talmage: What we think happens is that the antigen gets into the lymph nodes where the lymphocytes are, and it comes in contact with both T cells and B cells. When it reacts with the T cells, they make a hormone, you might say, or a mediator, they call it, a mediator which stimulates the B cells that are there reacting to the antigen themselves, but they need a little help from the T cells to do their work. So it's a complex interaction of cells that's involved in this process.

Williams: There's so much "teamwork," quote, unquote, involved.

Talmage: Right. It is teamwork. Of course, it is a form of natural selection in the body that's similar to the natural selection that takes place in the origin of the species. You know, the origin of the species is due to diversity and selective multiplication of some members of the species and not of the others. So the species gradually changes.

I did a piece of work with Lee Hood in which we were interested in the amino acid sequence of the different gammaglobulins. I guess I should say, reminded

me that the antibody molecule is composed of a constant region and a variable region, and the variable region is what determines the specificity of the globulin, whether it reacts with the antigen or not.

I forgot exactly where I was, but what shall I say? We were talking about the diversity of lymphocytes and its selective growth in a way is similar in an abstract way to the natural selection that takes place in the origin of the species. That idea, before that, it was thought that antibodies were produced by some kind of tailor-adaptation of the construction of the antibody molecule, that there was just one basic antibody, but it could be formed in different ways, and that in the vicinity of the antigen the antibody was changed so that it reacted with the antigen. That was the idea before the selective theories came about.

But I think we have to give credit to Niels Jerne for the idea that all of the antibodies are just natural globulins that existed there before. An analogy I like to make is there are two ways of getting a key to fit your lock. You can have one tailor-made or you can just get a bunch of master keys and you try them all, eventually you find one that works. Well, the antibodies are like that. There's a whole bunch of different antibodies there already, or different globulins, and they have different reactivities randomly. Some of them accidently will react with measles and some of them with whooping cough or some of them with other things. So that concept, that antibodies are just natural proteins that have been selectively multiplied, was the new idea.

Williams: You're at the heart of that new idea.

Talmage: I think so. I think I can claim some of the credit for that.

Williams: Tell me about the balance between science and family life for you.

Talmage: Well, I found that I was able to do that without any trouble. My wife is an artist, and she has her own interests and I have my interests, and we were somehow able to get along just fine that way. She didn't tell me what to do with my science and I couldn't tell her what to do with her painting. [laughs]

Williams: And along the way you had children?

Talmage: We have five children and ten grandchildren.

Williams: What are they all doing?

Talmage: Well, I have one son who is a doctor, and he works at a local Denver hospital, the Swedish Hospital. I have another son who is an expert at computer software, and if you need anything, if anything goes wrong, I just give him a call, and he can work my computer over the phone. Somehow he's able to get on to my computer,

and if anything's not working right, he'll just fix it. It's just amazing what he can do. So that's the two boys.

Then we have three girls. One girl is a psychologist. She's still practicing locally. One daughter works for the state government, and the other one was a music teacher and administrator at the Denver Public Schools and is retired now.

Williams: You speak about your wife's artwork. What have you done over the years to have fun or extra pursuits or enthusiasms beyond—

Talmage: I was always a great tennis player. I did a lot of tennis, and that's how I probably ruined my knee, and it makes it very difficult for me to walk.

Williams: Are we leaving something unsaid here today, do you think?

Talmage: Well, I don't know what exactly you want, but I've enjoyed talking to you.

Williams: I guess the last question I have would be—and I think you've really answered this already, but let's say it again—what is the impact of work like yours on the average citizen?

Talmage: Well, I think immunology has had a tremendous impact on prolonging human life. Before the smallpox vaccine, smallpox epidemics would wipe out half the population. Life was very insecure. Then, of course, the discovery of the plague bacteria was a tremendous advance. We discovered that the problem came from the rats. The rats were carrying fleas, and the fleas would jump from the rat onto the human being, and people would get plague. Then it would spread from human to human, so we had these big plague epidemics.

At one time, I know when Isaac Newton was working on his theory of gravity, the university, Cambridge University, where he was working had closed down for two years because of a plague epidemic, and he had to stay home. While he was home during those two years, he worked out three important theories. One was the theory of gravity, one was the theory of light, that white light is composed of colors, a light of many different colors mixed together, and he also invented the calculus. He did all that in those two years while he was home because of the plague epidemic.

But the point was there was one big epidemic that wiped out at least a third of the population of Europe. It was around 1350. All of this discovery of immunology of how to vaccinate against diphtheria, to prevent malaria, and the most recent epidemic has been the AIDS virus and the AIDS epidemic. They were able within just a few years to determine what caused it and how it was spread. So that's how immunology impacts human life. You know, AIDS is now being treated successfully. Although never cured, it is under control so that the individual who was treated with the AIDS medicines no longer are contagious.

So at least it blocks the spread of the disease a great deal. That's an example of how immunology has had an impact on human life and people live. Even just a hundred years ago, the average lifespan was between forty and fifty years, and it's now between eighty and ninety. Many people are living to be a hundred these days.

Williams: One more question. You retired in '88.

Talmage: Right.

Williams: But you have continued to conduct scientific research. Talk to us for a moment about that.

Talmage: Well, I haven't actually done research, but I've studied the scientific philosophy of physics. I've been interested, trained as a biologist. Biologists base their science on causal realism. That is there's only one reality, there's only one DNA code, there's only one life history of mankind, and our studies are based on an idea that the tubercle bacillus is a real thing. It's not just a mathematical concept. It's a real living thing.

I'm amazed to find in physics that there isn't this same interest in reality. It's more concern about finding mathematical equations that describe observations, which is good. I mean, with physics they are able to predict when there's going to be a sun eclipse, or they're able to predict how fast you have to go on one of these spaceships to take off from the Earth and go to the moon and they're even thinking about going to Mars. So a lot of good things have come from it, but I think the failure to consider the reality behind all of this has slowed down the development of physics and we haven't seen the revolution in physics that we've seen in biology. I mean, that's my personal opinion.

Williams: Thank you very much.

Talmage: Well, thank you for your questions.

[End of interview]