



The American Association of Immunologists Oral History Project

Transcript

Jonathan Sprent, M.B.B.S., Ph.D.
May 10, 2015
New Orleans, LA

Interview conducted by
Brien R. Williams, Ph.D.

Transcription: TechniType Transcripts
Transcript copy editors: John S. Emrich, Ph.D., and Charles L. Richter, M.A.
Final edit by: John S. Emrich, Ph.D.

© 2016 The American Association of Immunologists, Inc.

Publicly released transcripts of The American Association of Immunologists, Inc. (AAI) Oral History Project are freely available for non-commercial use according to the Fair Use provisions of the United States Copyright Code and International Copyright Law. Advance written permission is required for reproduction, redistribution, and extensive quotation or excerpting. Permission requests should be made to: The American Association of Immunologists, 1451 Rockville Pike, Suite 650, Rockville, MD 20852.

To cite an interview, please use the following general format: [Name of interviewee], interview by [name of interviewer], [date], The American Association of Immunologists Oral History Project. <http://www.aai.org/OHP> (accessed [date]).

Williams: This is an interview with Dr. Jonathan Sprent for the American Association of Immunologists (AAI) Oral History Project. Dr. Sprent is professor and head of the Cellular Immunity Laboratory at the Garvan Institute of Medical Research. He was President of the American Association of Immunologists from 1998 to 1999 and served on the AAI Council from '93 to '98. He was awarded the AAI Lifetime Achievement Award this year. We are at the IMMUNOLOGY 2015™ in New Orleans, Louisiana. Today is Sunday, May 10th, and I am Brien Williams.

Delighted that you are with us today, Dr. Sprent. Let's start with tell me—go back as far as you want to with your family.

Sprent: Okay. Well, it's a convoluted story, so I'll begin at the beginning. So I was born in England, 1941, in the north of England in Leeds, and then the family moved quite quickly to the south of England, to Chichester, which is on the sea. I lived mostly with my mother at the time, because my father [John F. A. Sprent], who was a veterinarian, as part of the War Office, he was sent by the British government to do some veterinary work on cattle diseases in Nigeria. So he spent most of the war years in Nigeria, so I hardly saw him as a young child. I will, as I go along, mention my father repeatedly because he did actually have quite a marked influence on how I ultimately came into science. So he worked on diseases of cattle, as I mentioned, and he became particularly interested in parasitic diseases, which became his specialty, and he ultimately became a parasitologist.

At the end of the war in 1945, he went back to Britain and he handed in his research from Africa in the form of a Ph.D. thesis, which was granted, and he decided he wanted to do academic parasitology as a career, but, unfortunately, in Britain at the end of the war, the country was broke, there was certainly no money for research, and, as you probably know, rationing in Britain lasted until 1950 or so. So an academic career in Britain was impossible, so he looked around for some other country to make a career in science.

So he chose the USA, and in 1946, I think, he moved to the University of Chicago, which was a center of parasitology in those days. The next year, I and my mother and my younger brother joined him at the University of Chicago. So I could well have grown up to be an American from that point on, but it didn't work out that way because he actually did very well, in fact, so well that he was offered a permanent position at the University of Chicago, but in those days, they had this strange rule that if you had a permanent job in academia, you had to be a U.S. citizen, and that would have meant he would have had to relinquish his British citizenship, and he didn't want to do that. So, basically, the USA was out, so he had to look around for somewhere else.

So he looked at Canada, and, in short, the next year the family was moved to Toronto, so that's where I spent my childhood. So I became a little Canadian, became involved, as little Canadians do, in ice hockey and baseball, et cetera.

And my father, he did very well in his career in parasitology, but then in 1952 or so, after five years in Canada, for reasons which I can't quite remember, he decided to take the whole family to the other side of the world, so we were moved from Toronto to Brisbane in Australia. So I was ten at the time, so I then had to give up baseball and ice hockey and learn cricket, pretty terrifying for a ten-year-old. [laughs]

But I must say I enjoyed life in Brisbane. So I went to school there and high school, and then I had to decide what I was going to do, and, as I say, I was much influenced by my father because he used to talk to me as a young child about, well, life in science, and how he was very interested in parasites, particularly in nematodes, where a small animal like a rat that's infested with a nematode gets eaten by a larger animal and then it reproduces in this animal and that then gets eaten by a larger animal, et cetera. So he was very interested in this, and I decided that I would like to do something like that, because he was saying that—and I would ask him, “Is this of any use?” And he'd say, well, that wasn't his prime consideration. He just found it interesting, and he was able to tell me that—and not only was he able to do this, but the government and the general public supported the idea that scientists could do things purely out of a sense of curiosity. And I thought, “Wow, that's not a bad life.” So I, too, decided to become a scientist.

So I decided that I wouldn't go to veterinary school as my father did, but, in fact, I went to medical school. So I went to medical school in Brisbane, and in those days, the medical school course was a six-year course, so you went straight from high school into medical school. These days, it seems to get into medical school you have to be pretty well a genius, because it's so competitive to get in. But, in fact, when I was admitted to medical school, as I remember, there were about a hundred slots available, and there were eighty applicants. [laughs] So I didn't have any problems getting in. Actually, the failure rate in those days was pretty high, but I managed to get through medical school without any problems. I certainly didn't have a distinguished career at all, and that was partly because in those days, whereas now in medical school you have exams all the time and it's extremely competitive, in those days there was one exam per year, so you'd spend three weeks studying and the rest of the year you could basically do what you wanted. So that's when I did my growing-up. [laughs]

Then the question came, so what would I do after I finished med school, would I actually be a practicing physician, and there there were two things that influenced me which I should mention. The first was in 1964, I think it was, I heard a lecture by Jacques Miller, who I will come back to in a moment, who, 'round about 1961, had published his crucial work on the function of the thymus, and I was extremely interested in what he talked about, which was basically that the thymus is the source of what we now call T cells.

So I heard this lecture, and then I finished medical school and I did a year as an intern doing various aspects of medicine, a bit of surgery, a bit of gynecology, psychiatry, and so on. But one of the things that particularly disturbed me when I was doing pediatrics is that I was looking after children with leukemia. This was in the '60s, and at that stage, drug treatment, chemotherapy for leukemia was in its infancy, and it would work and so children would be treated with drugs and they would generally go into remission, and they and especially their parents would be absolutely delighted by this miraculous diminution of symptoms, but they would always come back and they would always die.

And I, at the time, found it difficult to justify what seemed to me experiments on children, and so I decided that I just didn't really want to have a career in medicine. I decided I preferred to go what we now call back to the bench to understand, you know, to try to get a basic better idea of why these drugs didn't work as well as they ultimately did. And, of course, this is ironic, because treatment of childhood leukemia is now one of the great triumphs of medicine. It's been extremely successful.

So I decided that I wouldn't be a practicing physician. I would, instead, do basic research, and so I applied to do a Ph.D. after I finished my medical course, and I applied to the Walter and Eliza Hall Institute in Melbourne, which was and still is the main center of immunological research in Australia, and that is where Sir Macfarlane Burnet had recently been the director, and, as you know, he ultimately got the Nobel Prize sometime later [Ed. 1960]. And I went to work with Jacques Miller, who, as I say, I'd heard his lectures some years before.

So that sort of concludes my childhood, so the next stage of my career is, well, what happened next. So shall I—

Williams: Just before we go to next, I'm curious, do you have any recollection of the war?

Sprent: Of the war?

Williams: Mm-hmm.

Sprent: I don't. I do remember my grandmother telling me that when she went out into the fields surrounding the house that I lived in, the house, she was machine-gunned by German pilots. I mean, all the bullets missed, but she talked about the bullets pecking the ground all around her, and I must say as a child that totally terrified me. But I was not in an area that was subject to bombing, et cetera.

What I do remember is the fact that food was very, very limited, and I remember my mother talked to me about—well, she used to—I had one egg per week. That was basically all that was possible in those days. And she told me stories of how there was such a thing as a meringue, where you would actually take eggs and you would remove the yolk, and you would mix the egg white, you know, multiple

eggs, and the idea of multiple eggs mixed together, as a four-year-old child, this was amazing to me. [laughs] But other than that, no, I don't have any—I was too young, really, to remember the war.

Williams: And what was the British military's interest in the cattle study of your father's?

Sprent: I actually have never been quite clear on that, but apparently the economy of Nigeria was suffering very badly from diseases of cattle, and I think it was for economic reasons that they decided that they had to try to cure these diseases. Whether that was successful or not, I don't know.

Williams: And what was your feeling about being uprooted, well, eventually from Toronto and sent to Australia? Was that difficult for you or—

Sprent: I think, as for all children, it is a shock when it happens, and I was not an outgoing child at all, so I found it rather traumatic, and moving from one country, particularly to Australia, where foreign accents were a source of fun, I mean, this was sort of difficult to come to grips with. So I lost my Canadian accent pretty quickly. [laughs] But after a while, I was fine.

Williams: That's interesting, because you were at the age where you could adapt an American accent quite easily and the Canadian and then finally the Australian.

Sprent: Yes, indeed, yes, yes. As you see, I haven't kept much of my Canadian accent.

Williams: [laughs] Well, that's interesting. Your current accent is by choice or by environment?

Sprent: It's no choice involved, so it's probably a peculiar mixture of goodness knows what.

Williams: [laughs] Well, it sounds pretty British to me.

Sprent: Perhaps, yes. It's not typically Australian.

Williams: Right, right. All of these moves and different countries and so forth, did that have any determination on your personality, your outlook on life or such, or not?

Sprent: Well, I think the more you move, the more you are able to adapt to new situations. That sort of comes with experience, so perhaps that did apply to some extent, because I then subsequently moved quite a few more times.

Williams: [laughs] That's coming, I know. All right. So we left it with your having achieved your Ph.D.

Sprent: Yes.

Williams: And at that point, did you see a clear path ahead or were you still sort of checking out the field?

Sprent: No, I didn't really see a clear path ahead, except that what I do remember is that while I was medical school, I was generally bored. As I say, medical treatment itself, I felt there was too much experimentation involved, and lot of the medical problems that I ran into were actually social problems, you know, wives getting beaten up on a Friday night after payday and so on, and these were things that I, when I used to go to the emergency section of the hospital, there was nothing I could do about these social problems, and it was for that reason that I moved away from clinical medicine. But once I started my Ph.D., and this was really my first experience in science, then everything changed.

Perhaps, by the by, I could, talking about research experience, come back to what I used to do in the summer vacations when I was a medical student. So I had some interesting jobs there. One of them was to do pregnancy testing of women, and in those days the typical way of measuring pregnancy didn't exist. Instead, you'd inject the urine of a woman who thought she was pregnant, into a toad, under the skin of the toad. Then you would look in the urine to see spermatozoa. This was the standard pregnancy test in the 1960s.

Williams: You weren't looking at the frog's urine; you were looking at the women's urine.

Sprent: You would inject the woman's urine subcutaneously in the frog, and then you would look at the appearance of—I guess it was sperm in the urine of the toad. [laughs]

Williams: A two-step process. Huh.

Sprent: So I did that for a while, and then I used to trap rats for my father in the jungle, because he was interested in parasites and how they were transferred from one animal to another. So one of my jobs was to set traps to catch live rats, et cetera.

And then—this is actually an interesting anecdote—my father had been much influenced by the work of Jacques Miller, who I should mention, and this is well known to immunologists, that if you remove the thymus from a young mouse, then it will get sick because it doesn't have any T cells. We now know that's the reason. So my father was influenced by this, and he wanted to know whether removing the thymus from a young or newborn rat would have any effect on parasitic growth. So he said, "Well, why don't you learn how to do thymectomies." So he had a recipe that Jacques Miller had sent him about how to do thymectomies, and so I learned how to do this. I had to teach myself. Are you a scientist yourself?

Williams: No.

Sprent: Well, actually, thymectomy is quite tricky. You have to remove the thymus, which lies below the bone here in the front of your chest. And in a newborn mouse, the thymus is actually quite large, so you can remove it and then you can put a couple of stitches in, and that's really all there is to it. So it looked very simple in the recipe. So I learned how to do this and I thymectomized hundreds of baby mice. I thought I was actually pretty good at it until one day I actually did histology, and I looked at the section of what I had removed under the microscope, and I found, to my horror, that I hadn't been removing the thymus at all. I'd been removing the salivary glands, which are up here in the neck. [laughs] So I had hundreds of rats that didn't have salivary glands, but eventually I did teach myself how to do this. [laughs]

Then I found, interestingly, that when these neonatally thymectomized baby rats were infested with a parasite. Parasites typically caused the appearance of a particular blood cell called eosinophil, which is a sign of allergy. And I found, in fact, that these thymectomized animals didn't develop eosinophilia, and this was actually a novel finding at the time, but we never wrote it up. In fact, we should have done, because this was really the first evidence that the thymus actually has an effect on this particular type of blood cell.

But this experience with practical immunology stimulated me to actually want to study the immune system. So, as I say, when I did eventually start my Ph.D. work, I sort of really fell in love with it, with science, and I decided, well, this really is my career. So I then had to look around for where am I going to do it. In those days, it was a tradition in Australia that you would do your postdoc in some other country. You wouldn't do it in Australia. And it so happened that my boss, Jacques Miller, for his sabbatical decided to go a new institute in Basel in Switzerland, and this was right about 1972, and this was the Basel Institute for Immunology. So, in short, he said, "Why don't you come along," and so I did. As soon as I finished my thesis, I went to the Basel Institute. So perhaps I could take a few minutes to talk about the Basel Institute.

Williams: Please do.

Sprent: So the Basel Institute was founded by a drug company, Hoffman-La Roche, and the initial director was Niels Jerne, who ultimately got the Nobel Prize a few years later [Ed. 1984]. And it was an experiment, and the idea was that it was an institute of about fifty or a hundred people, and people would be recruited, whether they were postdocs or whether they were relatively senior people, and each staff member would be given one technician, and that was the size of your group, you and a technician. It didn't matter how senior or how junior you were. And that's how it worked.

So I joined there, and it was a tremendously cosmopolitan group of people from Sweden, from Europe, from Australia, from the United States, and it became a

training ground for immunologists all over the world, probably trained five hundred people, and many of the people here at this meeting had some experience at the Basel Institute. The great thing about it is you didn't have to write any grants. The money came entirely from Hoffman-La Roche, but they placed no constraints on you on what you wanted to do. They gave you money. If you ordered equipment, say, an ultracentrifuge, which is a very expensive piece of equipment, the only question was it one or two you wanted, whereas now that would totally unheard of. So you didn't have to worry about money, there was nobody to tell you what to do, and so you could do basically what you wanted to do. If you went skiing for a month, nobody would care. You didn't have to sign anything. It was basically total freedom, and it was actually paradise. And I think a lot of the people who worked at the Basel Institute over the years had the same experience that I did.

Now, I was one of the very few people who had decided—and this was influenced by my father—that I wanted to get into science partly as a way of seeing the world. So he'd been to many, many foreign countries, and he used to go to very exotic countries. I didn't get to too many exotic countries in my career, but it was basically a way to see the world. So I decided that I would spend only two years at the Basel Institute, and I thought, well, next step will be my birthplace, so I went to London. So I then spent two years at University College London. And I could spend a couple of minutes talking about that.

Williams: Please do.

Sprent: This was a completely different experience. Whereas the environment at Basel was perfect for doing science, et cetera. University College when I was there was not like that at all. They had very little money. The animal colony was appallingly infected with all sorts of diseases, to the extent that every year they used to have to kill all the mice, fumigate the place, and then start again. Otherwise, you couldn't do any experiments, because the mice were too infected. Now, of course, all animal colonies are incredibly clean and you don't have this problem. But it was actually very difficult for me to do very much work there, even though I enjoyed life in London. British though I am by birth, it was really just that two years that was really my only experience of actually living in Britain that I remember.

So then what did I do? Well, it turned out that when I had handed in my Ph.D. thesis in 1972, one of my examiners was Darcy Wilson, and he was one of the well-known immunologists at the University of Pennsylvania, and I met him in the south of France at a meeting once. He had read my thesis and he'd enjoyed the experiments that were listed there, and he said, "Why don't you come to Penn." So, in short, after I finished work in London, I was recruited to the University of Pennsylvania, so that was my next move. [laughs]

So I'll tell you a little bit about Penn then. So Penn was—this was really my introduction to America, as I remember it, and this was, to me, a wonderful experience, and I'd ultimately have thirty years in the USA, which I enormously enjoyed. And I think many immigrants to the U.S. have had the same experience, that this was a country where basically you're on your own and it's up to you, and everything is there if you have the nous to make the most of it. And I thoroughly enjoyed life there. This was my first experience for some time since I had left Melbourne of being in an academic environment with students, et cetera, so I had my own graduate students and postdocs, et cetera, and so I lived a very pleasant academic life at the University of Pennsylvania for about eight years or so.

In those days, the University of Pennsylvania was, I think, just about the first medical school built in the country. It was built before 1800, I think, and the physical plant reflected the fact that that's when it was built, and it was pretty, pretty bad. [Ed. The University of Pennsylvania School of Medicine was founded in 1765 and moved to current location in the 1870s.] The animal house was pretty awful. And as time went on, even though I enjoyed life in Philadelphia, I became increasingly dissatisfied with, well, the fact that experiments, which depend very much on having clean mice, I just couldn't do these experiments.

So I looked around for somewhere else to go to, and so I started to look for jobs, and I ultimately looked at a job in California at Scripps [The Scripps Research Institute]. Then, of course, whenever you think about moving, you think about there are pros and cons about any move, and there's always something that sort of tips you one way or the other. For me, the tipping point, I vividly remember, was on a Sunday afternoon I was actually in my office at Penn, and my office was immediately under the animal colony, and above the animal colony was a roof, and it was raining, and the rain came through onto the animal colony, and all this yellow water dripped all over my desk, all over my books, and I decided, "No, it's time to move." [laughs] And so I moved to a new life in San Diego.

Williams: Amazing, amazing. At what point did the laws of America change so that you could practice science in this country, or did you become an American citizen?

Sprent: In those days, you had to, as you do now—the rules then were much as they are now. You apply for a visa, and there's choice of various types of visas. I applied for—well, I have what's called a J-1 visa. It's not really important. And then after three or four years, you then have to decide what you want to do, and generally these visas were for a brief period and then you had to go back to your home country.

Now, it just so happened in Australia when I decided to move overseas, I didn't have a passport, and I actually was able to apply for two passports, a British passport and an Australian passport, so I was actually granted both of them simultaneously. And by chance, I used my British passport to enter the USA. Now, that was actually a piece of pure good luck, because it meant that on my

visa after three years, I could apply immediately for a green card, whereas if I'd used my Australian passport, I'd have been forced to go back to Australia for two years and then to apply. So this was a bit of luck. So I got a green card and, in fact, I kept that green card for twenty-five years, and then ultimately I became a citizen.

Williams: Well, what was it that prevented your father from staying at Chicago?

Sprent: Because in those days he would have had to become a U.S. citizen and would have had to give up his British passport.

Williams: So the whole system had changed in the interim.

Sprent: It had changed, yeah. So dual nationality was something that came in much later. But, as I say, for a long time in the States I was there on my British passport. I just had a green card.

Williams: At some point did you acquire a family in these days or is that—

Sprent: I did. I was married to somebody I knew in Australia, and she moved with me to Britain, so we had two kids there. And then we moved to Philadelphia, and then, sadly, my marriage sort of fell apart, and the two children, with their mother, went back to Australia, and they all moved, actually, to Hobart, which is in Tasmania, this island south of Australia, and so that's where they live there.

I was then ultimately sometime later married again, I can briefly mention, to Sue [Susan R.] Webb, who is from Alabama. We met at Penn, and then she moved with me to San Diego. We were married for quite a few years, and we had a very good—well, we had a good marriage and we had a good academic relationship because she's also a scientist, and so it was mutually beneficial for both of us from a scientific point of view.

Williams: Was she also at Scripps?

Sprent: She was also at Scripps, yeah, where she also ultimately rose through the ranks and became a professor there too.

Williams: Interesting. So now give me the portrait of Scripps at the time.

Sprent: Scripps at the time. I should point out there were two Scripps. There's the Oceanographic place, and there's The Scripps Research Institute, which is where I went to, and it's a private research institute, one of the biggest in the country. People in the USA are fully aware of this, but people outside in other countries are unaware of how a place like Scripps could have arisen from nothing in 1950 to an institute with three thousand people in a period of forty years, and the way that happens is because of indirect costs on grants. So, in other words, Scripps

got started by a man named Frank Dixon, who ultimately became president, moving, I think it was from [University of] Pittsburgh with a group of postdocs, and they all rose through the ranks and they all got their own grants, and each grant brought in overheads. And the overheads at Scripps were 90 percent or so. And with that money from overheads, Scripps was able to rent buildings and recruit people, and it just grew exponentially. This is the way science has always worked in the U.S., and this is unique. It doesn't happen anywhere else, because overheads on grants are not nearly as generous as they are in the USA. So that's how Scripps was able to go from nothing to this enormous institute in such a brief period of time.

It was a very invigorating place to work, and I made lots of friends there, and work went well and I flourished and thoroughly enjoyed life in San Diego. It didn't have the advantage that Penn had of having access to graduate students, because Scripps was not really a university. So one had to function on postdocs rather than graduate students, which is somewhat different, but still it was a great place to work and a great place to live.

Williams: I thought there was a tie-in with UCSD [University of California, San Diego]. No?

Sprent: Well, people had adjunct appointments at UCSD, but they were basically two separate institutes, et cetera. Sometimes people at Scripps would do a bit of teaching at UCSD. I, myself, didn't do that.

Williams: Was your campus in La Jolla?

Sprent: It was in La Jolla, yes.

Williams: Did you take up hang gliding while you were there?

Sprent: I didn't do any hang gliding. [laughs] No. I lived in North County, which I much enjoyed, on the coast.

Williams: A special place.

Sprent: It is. It is indeed, yes.

Williams: Right, right. So you were there until when?

Sprent: I was there until 2006, and then at that stage, I was about sixty-five or so, and my father was getting old, and I began to think about moving back to Australia in his declining years and also to be closer to my family, et cetera. So I began to think about returning to Australia, and then ultimately I applied for a large grant that was offered by the Australians, and this was quite lucrative, and it made it possible for me to move.

Also ‘round about 2006, and it’s not much better now, the NIH [National Institutes of Health], the funding system, the proportion of grants getting funded had dropped to extremely low levels. It was less than 10 percent, and I think it’s not much better than that now, and this made science an ordeal to some extent. So scientists, when I first went to the States, you wouldn’t spend very much time writing grants at all. Ultimately, people spent a huge amount of time writing multiple grants, and this, to some extent, took the fun out of doing science, so I was hoping that the situation would be a little easier in Australia, which it has turned out to be.

Williams: Did your parents come and visit you much in the States while you were here?

Sprent: They did now and again, yes. They made actually multiple trips, firstly to Philadelphia and then to California.

Williams: Did your father express pride in your progress?

Sprent: Yes, I think he did, yes. I actually grew much closer to him as he got older. I suppose this often happens. When he was young, he was a pretty dynamic person. He was dean of the veterinary school [of the University of Queensland] at the time, so he was always very busy. But as he got older, I became much closer to him. And I think I hadn’t mentioned that when the family had moved to Brisbane, that he, I think largely guided by my mother, had decided not to live a suburban life at all, but, in fact, they bought a farm of 120 acres which was just outside Brisbane, to the extent that it was a thirty-minute drive for my father to get to work. So it was quite possible to commute from this what was, in effect, an idyllic life in the countryside, this big property where he ran cattle, et cetera, on the river. So I had sort of the best of both worlds, really. So I used to, when I was in California, I would travel several times a year back and spend some time on the farm.

Williams: So what was it like being back in Australia then as a professional?

Sprent: You mean when I ultimately returned?

Williams: Right.

Sprent: Well, it took quite a bit of readjustment, actually, because I had become Americanized and I was used to the way science is done in this country, which I admire and had got used to, and it was not quite like that in Australia. There were subtle differences which I ultimately got used to.

Williams: Explain some of those differences.

Sprent: There is a lot more bureaucracy involved in science in Australia. Grants, even though more grants get funded, they're much smaller, so you'd actually have to spend more time writing grants and so on. So there were subtle changes, but I'm now used to it.

Williams: So the terms on which you accepted this new position was that you were to create a lab, or were you just stepping into an already existing system?

Sprent: Well, actually, it was a slightly odd situation. I was recruited by Tony [Antony] Basten, who was a colleague of mine when I was doing my Ph.D. He was a postdoc with Jacques Miller and I was a graduate student. So we have known each other, well, since 1960s. He was head of an institute in Sydney, and he recruited me there. He said, "Why don't you apply for this big fellowship," which, as I mentioned, I got, and that allowed me to move to that institute and start a group. But just after I arrived, he decided that he would move to another institute in Sydney, to the Garvan Institute, which is where I am. So he and his group decided to move, and so I more or less went along. So I only spent just a few months at this initial institute.

Williams: That kind of behavior was acceptable to the initial institute?

Sprent: Oh, it's one of these—it happens. I mean, it's nothing uniquely Australian about that. [laughs] It could happen in this country just in the same way. But the two institutes, they were similar, actually.

Williams: And what was the status of Gavin [Ed. Garvan] at the time? Was it new or—

Sprent: The Garvan Institute was founded, I think, in the 1960s or seventies [Ed. founded in 1962, opened in 1963]. I'm not quite sure of its history. And it is a private research organization, much as Scripps was, and it's affiliated with the university, so there's access to students there, and it was similar to Scripps in the sense that one is dependent entirely on grant support, just as applied at Scripps. And I should mention that at Scripps, one of the problems with Scripps is that because the whole structure of Scripps depended so much on overheads on grants, there is only one granting agency in the U.S. that pays the 90 percent overhead that's necessary for a place like Scripps to run, and that's the National Institutes of Health. So other sources of funding like the National Science Foundation and so on, they don't pay anything like that; it's more like 20 or 30 percent. So at Scripps we were not allowed to apply for these grants. We had to rely only on NIH grants, and that made it actually very difficult.

Williams: In what way difficult?

Sprent: Well, difficult because when the funding rate for grants at the NIH went down, it means you couldn't apply to other granting agencies. We simply weren't allowed to do it. Whereas at other institutes around the country, you could do that, and

you could pick up sources of money from arthritis places, multiple sclerosis, and grants and so on, but you couldn't do that at Scripps.

But in Australia, the overhead on grants is nothing like 90 percent; it's more like 30 percent. So this is a big problem for institutes in general in Australia, so they cannot grow as American institutes can grow, so they tend to remain much smaller. So Garvan is not a large institute. It's relatively small, even though there are many different types of science that go on there.

Williams: What is its mission or—

Sprent: It's medical research, so there's cancer and diabetes and immunology. Much as what happens in major universities here, at Scripps was much the same.

Williams: Did you bring people with you from the U.S.?

Sprent: I did bring some postdocs with me, yes, and they remained with me for some time.

Williams: And then you've also—tell me about this South Korean connection that you had. Or is that just a very minor thing?

Sprent: Yes. So one of my postdocs at Scripps is Charles Surh—everybody calls him Charlie—S-u-r-h. And he did very well when he was with me, to the extent that he rapidly became independent and rose to become a full professor, and we had a very good collaborative interaction for quite a few years at Scripps. And then because of his Korean connections, the two of us were invited to spend some time at a small town in Korea called Pohang, which is on the southeastern coast. In short, the reason that this came about is that South Korea is very keen to get a Nobel Prize because it doesn't have one. [laughs] And it had decided that science was the best way to get a Nobel Prize, and they put all their eggs in a basket of a person who, unfortunately, was found to have committed fraud, a stem cell person. I won't go into details about this, but this was a huge scandal.

But, nevertheless, the government decided that putting money into research was the way for Korea to get a Nobel Prize, so they decided that the best way to do this was to increase the standard of science in Korea. So they decided to put a lot of money into a program that would bring visiting investigators in. So I and my colleague Charlie Surh, as well as many other people, mostly from the States, were invited to join various universities in South Korea and spend a period of some months a year there. So that's what I did for a five-year period.

Williams: I guess we should move on now to talking about the highlights of your science, what you're going to be remembered for.

Sprent: Well, I'm still working on those. [laughs]

Williams: Well, I was just thinking I didn't say that—that didn't come out quite right.

Sprent: Highlights of my career. Well, I've always considered myself a bit of a dabbler. I don't have any great mission in science. I'm in science—and this is influenced by my father—out of a sense of curiosity. So I find myself doing things that catch my fancy, so I'm interested in this and then I move from this to that, purely out of a sense of curiosity.

So I've done many different things in immunology, mostly centering on T cells, working on thymus, where T cells originate, working along with many other people on how the thymus actually functions. This paradox that the thymus is an enormous organ in young people, in babies, and yet of the cells that are produced in the thymus, something like 95 percent die, which seems very wasteful. And we now know this is actually a reflection of a highly sophisticated program of what's called thymic selection, that selects a particular set of T cells that function in your own body that's different from cells generated in another body. This was of great interest to me, as well as to other people, to understand how this happened.

Then, of course, when the cells come out of the thymus, they live for a long time. I was interested in how long lymphocytes do live for, which is actually quite a long time, most of them, and what is it that keeps them alive and where do they go and how do they function, what is needed to cause a T cell to respond to some infection and so on.

Then I've also been interested—and this is going back to the fact that I graduated in medicine. I have interests in applying what has come from studying mice, things that might be of some use to human diseases. So I was interested in transplantation immunity for quite some time, bone marrow transplantation, problem of graft-versus-host disease, et cetera. And then cancer immunotherapy is one of the things that I'm particularly interested in now.

Williams: So where are you looking now?

Sprent: Well, now I'm trying to—one of the things about cancer is there's always been a vague hope that the immune system is useful for cancer and that there's been quite a lot of evidence that it's useful to some extent for certain forms of cancer, but in the last two or three years, there's been enormous number of breakthroughs that the immune system really is important for cancer, and if you can boost the immune system in different ways by novel techniques that have only recently become available, you actually can cause quite significant remission in a series of tumors, and that's all pretty new, and there's a lot of excitement now and in the future about new ways to treat cancer.

Williams: And where is your work leading you at Gavin [Ed. Garvan] in that area specifically?

Sprent: Well, I work entirely in mice, and I have done throughout my career, even though I was trained to be a real doctor. [laughs] But, you know, you have to start off with work in animal models, and then you hope that what comes from studies in mice will ultimately apply to humans, and sometimes it does and sometimes it doesn't. So right now we're trying to find ways to boost the efficiency of the immune response to cancer cells in rather complicated ways, which I probably won't get into, but suffice it so say that that's one of my main interests right now. But, you know, I'm right at the end of my career now. [laughs]

Williams: And do you have successors primed and ready to go, is that not the way your science works?

Sprent: You mean people that I've trained, et cetera? Well, yes, but this, I think, works with everybody, you know. I mean, it's years since I, myself, actually did any raw science, but people come through your lab, and the best ones go on to bigger and better things, and they become independent investigators and they shine on their own. So, yeah, I've been fortunate to have quite a lot of people who've been through my lab who've done extremely well since that time.

Williams: Right, right. Let's talk about the AAI for a few minutes. You became a member in 1980, I think it was.

Sprent: Yes. I don't actually remember joining it. I think I largely joined it because in order to get *The Journal of Immunology* [(*The JI*)] cheap, then you had to become an AAI member. I think that was my main reason for joining. [laughs]

Williams: But that indicates that *The Journal [of Immunology]* was important to you and your work.

Sprent: Yes, yes, it was indeed.

Williams: So did you become active in the organization before you became president?

Sprent: Well, the way it works—and you've probably heard this from previous presidents—is that you get elected to the council, and it's generally—well, you know this better than I do. Usually three names are put up and then the whole membership votes on this, so I was selected and joined the council. You know, you rise up through the ranks and eventually you think, "My god, I'm president." [laughs]

Williams: Did you bring along with your work through the council particular issues that you felt were very important?

Sprent: No, I didn't, actually. No. I was pretty impressed with the way the council was functioning, I must say, although in those days, in the early 1990s, whereas the

AAI now has very substantial reserves, financial reserves, in those days it didn't, and we were always sort of on the brink of being broke, I think it was. So there were some difficult times in those days. [AAI Executive Director] Michele Hogan joined 'round about the same time I did, and she was an enormously important recruit to the AAI, so I much enjoyed my interactions with her.

Williams: So you were president 1998 to '99.

Sprent: Yes, right.

Williams: Talk about the tenor of those years. That was George H.W. Bush [Ed. William J. "Bill" Clinton]. What was funding like at that particular point from NIH? What was it like?

Sprent: Well, you probably missed a spoof that I did the other day. [laughs]

Williams: I didn't.

Sprent: This was for my presentation for the AAI. As I say, when I first joined the University of Pennsylvania, grants were very easy to get, so one in two grants were getting funded. Then it dropped to about one in eight grants, and that became very difficult. This caused anguish throughout the whole country. In fact, we've never quite recovered from it. It's just about as bad now as it was then. But soon after I joined the council, there was a big push to increase the size of the NIH budget, and ultimately it ended up by being doubled, and that certainly helped a great deal, but it also possibly—and this is arguable—had a negative effect, and that is that some people who probably should not have had their grants funded actually did get funded, and the end result was that once the NIH budget got doubled, politicians now had no more incentive to keep putting money into the NIH.

So since that time, since the year 2000, if anything, the amount of grant money in today's dollars has gone down, in fact quite substantially, and this has been a big problem. As I say, it's debatable whether doubling the budget was a negative effect or not. I think you'd get different opinions from different people about that. But it certainly was a problem.

Williams: You were quoted, I guess during your presidency, or perhaps not, as calling on the membership to barrage Capitol Hill.

Sprent: Was I? [laughs] I don't remember that. Yes, well, I think that was a reflection of what we as council felt in those days, that this was in the days when I think we were important for starting the push to get much more money for the NIH, which ultimately did happen. So that was beneficial.

I'll give you a little anecdote about the budget, and this is before I was president. I was deputized by the political arm of the AAI to talk to my congressman about the importance of not targeting money entirely to what we would call translational directions; in other words, that there should be a substantial amount of money still being put into to basic research, curiosity-driven research. So I was deputized to talk to my congressman, who was Randy [Randall H.] "Duke" Cunningham, and Randy "Duke" Cunningham apparently was a fighter pilot in the Korean War [Ed. U.S. Navy pilot during the Vietnam War], and there were rumors that his exploits in Korea had something to do with the movie *Top Gun* that starred Tom Cruise, et cetera. So he was quite a character and he was a very influential person in Congress. He was on the Appropriations Committee, which had a lot to do with the budget.

So I was instructed by the person in the AAI whose role it was to interact with Congress, to talk to Randy "Duke" Cunningham about the important of basic research. So it was arranged that Randy "Duke" came to my office at Scripps, which completely terrified me, so I was very nervous about this. And then I was told that, "In fact, you don't have to entertain him. It's the other way around. He's a politician. He'll make *you* feel at home. You don't have to do that." And it turned out, in fact, to be exactly that.

So I remember he came to my office at Scripps, and I had assiduously cleaned up my office, make way for a congressman. When he came to the door of my office, he saw a microscope lying on the bench, and, brilliant politician that he was, to break the ice he said, "Doc, what sort of a microscope is that?"

And I said, "Oh." [laughs] I was completely taken aback by this. I said, "It's a Zeiss, a Zeiss microscope."

And he said, "Doc, I've got a Zeiss scope on my hunting rifle." So we then spent the next twenty minutes talking about hunting, about which I knew absolutely nothing, but this broke the ice and we became sort of loose, et cetera. And then I had to give him my spiel about the importance of increasing the NIH budget and making sure that the money was not put all into prostate cancer and breast cancer, et cetera, but into basic research. And I was stumbling my way along here, and he stopped me and he said, "Doc, I know the meaning of the word 'serendipity.'" So in practice, he already knew the importance of basic research. I didn't actually have to tell him. So I'd done my job. [laughs] And the end result was we ultimately got a lot more money.

Williams: Due to the congressman's efforts?

Sprent: Indeed.

Williams: Quite a triumph.

Friday night you received the AAI Lifetime Achievement Award. How does that make you feel?

Sprent: Oh, I was tremendously chuffed, as they say in England, pleased, honored. It's wonderful, I mean totally unexpected. Yes, I was blown away. Yes, wonderful.

Williams: And going beyond that, what is the importance of the AAI now in the field?

Sprent: In the field of immunology or—

Williams: Mm-hmm.

Sprent: Well, the AAI, it's indispensable for immunology in this country. It's enormously important. Not only is it the center of immunology, but it organizes a whole series of meetings, and it's the centerstone, and so the country couldn't do without it. Of course, every country has its society of immunology, its associations, but the AAI has been particularly successful, I think, in its function.

Williams: And I guess *The JI* is sort of the publication of record for the field. Would that be correct to say?

Sprent: Yes. *The JI* has a terrific history. It goes back to 1913, I think. I can't quite remember when it was first founded [Ed. first issue was printed in 1916.]. It's always been the basic journal. It's not the first journal that you'd send your papers to. Generally, you'd like your papers to go in very high-profile journals, but very often your chance of getting into those very high-profile journals is pretty limited because it's so competitive. So, ultimately, you decide to send your paper to *JJ*, and *JJ* has always been a very rock-solid journal, so there's a sense of pride in publishing papers in *JJ* for sure.

Williams: Right. Some sort of summary matters here. I'm struck by how much you've traveled around the world and been in all these various places and so forth. Is there something you can put your finger on in terms of the universality of immunization workplaces? Any lab you go into, is it sort of like any other lab, or is there not a universality of the workplace in immunology?

Sprent: You mean is very lab much the same? Is that what you mean? Well, the answer is yes, it is, actually. The labs throughout the world are structured with there's a boss and then there's a group of people working with the boss, and this can be a group of a hundred people or it could be a group of two or three. But the structure is much the same. And, of course, it's the students and the postdocs, the graduate students who do all the work. I mean, the boss generally does nothing. I mean, I'm thinking back on my career. I learned to do almost nothing in terms of practicalities in immunology. The only thing I did do—and I didn't mention this before—is I learned how to a surgical procedure, which is to place a cannula in the thoracic duct, which is the main lymphatic vessel in mice, and I did this. In

fact, I was very good at it. [laughs] It's the only thing in immunology I think that I was good at. I did it for quite a few years, so it's a way of collecting lots of lymphocytes, et cetera. So I collaborated with many people on the properties of thoracic duct lymphocytes, et cetera. And I should mention, in order to do these operations, I was a pipe smoker, so I would always be smoking my pipe as I used to do these operations. Not acceptable these days.

Williams: What are your thoughts on the future of immunology? Where do you see it going?

Sprent: The future of immunology. I think over the years there has been the pervasive hope that immunology is going to cure a lot of diseases, and I think that we're only at the beginning of this actually coming into fruition. So, in other words, if you think about vaccinations, I mean, vaccinations have been around for a very long time, and for acute infections vaccination works extremely well, and vaccinations were actually developed long before the age of modern immunology. But vaccinations for chronic diseases like malaria, for HIV, for cancer, et cetera, have been much less successful, and so there's great hopes that this will ultimately be successful, but so far, it has been a huge struggle, and that's where there's going to be a lot of emphasis placed in the future.

The same thing for transplantation. So I've had a long interest in transplantation immunity. So, for example, if you're ill and you need a kidney transplant, it's been possible to do this for the last fifty years, but you have to take drugs more or less for the rest of your life, because if you don't, then the kidney is rejected. There's been enormous effort to devise techniques for overcoming this constant necessity to take these immunosuppressive drugs which make you susceptible to infection, and this had been extremely difficult. There are ways to do it, and I'm much impressed by the work of David Sachs and Megan Sykes, who've been able to make this work under conditions where you don't need immunosuppression. So if you could devise techniques where you can avoid having to take these drugs, that would be tremendously important.

The same thing for treating autoimmune disease. I think basically knowledge in basic immunology has still a long way to go in terms of curing autoimmune diseases. So even though knowledge in basic immunology has grown exponentially over the years, the application of this to curing human diseases has, in effect, been much slower than one would have liked. I mean, you remember in the '80s when HIV first became—well, we first heard about HIV, there were all these predictions that a vaccine for HIV would be available within the next two years, and here we are thirty years later. So there's lots to do.

Williams: What about America's role in the field? Dominant? No longer dominant? What words would you describe there?

Sprent: America has been certainly dominant in the field ever since the end of the Second World War. Before that, it was, I think, Germans and so on. But since the war, science and immunology, which is what I know about, has grown up largely in this country, with a lot of input from certain other countries, too, but certainly the USA has been the leader.

Now, in the future, I think partly because the difficulty of getting funding in this country now for the last twenty years or so, the best young minds may now be having second thoughts about getting into immunology, into science, because it is a precarious career. So there's a risk that people will move away from science, which would be an enormous pity. And it's quite clear that there's been a great move, particularly to China, in the recent years. I mean, China has grown enormously in terms of its impact on science. So the question is, will science move gradually from the USA to other countries, particularly China? I think that remains to be seen and I think it's going to depend to a great extent on recovering funding in this country. If the NIH can boost funding so that one in five grants are funded rather than one in twelve, that could make a huge difference.

Williams: I looked up your lab at Gavin [Ed. Garvan] and was surprised to see that all but two of you appear to be of Asian background.

Sprent: In my own laboratory, that's true, yes. I've been particularly lucky with Asian people. I don't know quite why they pick me. [laughs] But on the other hand, if you think about labs in the USA, it's much the same. I mean, there's been an enormous influx of Asians, particularly people from China, who come to this country and do extraordinarily well, and now they're getting recruited back to China.

Williams: Talk a little bit more about how you've mixed your private life, your family life, and your scientific career. I guess we sort of lost that a little while ago. Can you add to that portrait?

Sprent: Well, I think science is a pretty tough, tough life. I mean, it's so preoccupying that it can make personal relationships difficult. I've been married several times, and I think part of the problems that I've had is that science dominates so much of one's time that personal relationships do suffer. Other people—and I have great admiration for these people—manage to make it work extremely well. I think it depends largely on one's personality.

Williams: So you had no other children beyond the two that—

Sprent: No.

Williams: Right, right, right. In another lifetime, would you still have chosen science?

- Sprent:** In another lifetime. Yes, I think I probably would, because I can't think of really anything else that I could do that would give me the sense of satisfaction of being able to—I mean, the great thing about science is you spend so much time thinking about problems, problem solving, and that's what I need. I need the stimulation of having problems to solve, which clinical medicine would not have done that for me. If I'd been more intelligent, I would liked to have been an astrophysicist, something like that, but my math was never strong enough to be able to do that. But science in general, I can't think of anything else that I could have done.
- Williams:** It's interesting you say that the clinician's life is not solving problems, but it is, of course, at the individual level.
- Sprent:** It certainly is, but I think clinicians—and my experience, of course, is very limited—is you do see some very fascinating clinical problems at times, but you also spend an awful lot of time seeing rather less interesting things.
- Williams:** Right, right, right. I've been asking everyone this question. Outside of the science, what do you do to have fun?
- Sprent:** Well, that, of course, raises the issue of what do you do as a scientist when time moves on and you have to retire, which is something that I'm trying to come to grips with now. What am I going to do? I mean, I'm seventy-four this year, so I can't keep going on indefinitely, and I won't. So I don't know quite what I'm going to do. Hopefully, we'll have other interests. I mean, what interests me now? I like to read. I'm very interested in classical music. I like to go to concerts. I appreciate gardening, et cetera, even though I don't have access to that now. And I have a grandchild who I adore, and I'm ultimately going to settle in Tasmania where I have my family, and that'll be yet another move which I'll have to get adjusted to. [laughs]
- Williams:** Do you see very clearly where you're going to be in Tasmania and so forth? Have you bought a farm?
- Sprent:** Well, no, I've bought an apartment in Hobart, which is the largest town in Tasmania, but it's only 300,000 people, but it has a university and so on.
- Williams:** This world traveler is going to go off to that island in the far south.
- Sprent:** But I never—I don't want to close any bridges, because the fact is I do have three nationalities. I often think about perhaps I'd like to come back to the U.S. to live. Perhaps I'd like to rediscover England, where I came from but which I really don't know as a place to live. I had a great time in Switzerland. I could perhaps go back there. So I'll probably do quite a lot of traveling.
- Williams:** I imagine that you are a man of many anecdotes. [Sprent laughs.] I don't know quite how to ask this. Are there a couple that come of mind of significant

exchanges with various people or some hilarious experience that you had at Scripps, or not?

Sprent: I'd have to think about that. I mean, I've given you several anecdotes now.
[laughs]

Williams: You have, and thank you. That's why I say there must be more.

Sprent: Yes, there probably are, but I can't think of anything that comes to mind right now.

Williams: Okay. So then I guess maybe we're done.

Sprent: Good.

Williams: Thank you very much.

Sprent: My pleasure.

Williams: Great. Thank you.

[End of interview]