



The American Association of Immunologists Oral History Project

Transcript

Richard W. Dutton, Ph.D.
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Williams: This is an interview with Dr. Richard Dutton for The American Association of Immunologists Centennial Oral History Project. Dr. Dutton is professor of pathology at the University of Massachusetts Medical School. He was president of the American Association of Immunologists from 1995 to '96 and served as an AAI Council member from 1990 to '95. He was awarded the AAI Lifetime Achievement Award in 2004. We are in a conference room in the Department of Pathology at the University of Massachusetts Medical School. Today is Friday, November 2, 2012, and I am Brien Williams.

Dr. Dutton, I'd like to start out by asking you to talk a little bit about your family background.

Dutton: Well, my father was a high school teacher in London, and I don't think my mother actually graduated from high school. Her father died, and she went home to run the household, so she never finished.

My grandparents on my father's side, my grandfather, I think, started out as an errand boy in Covent Garden in London and worked his way up to have what in England is known as a greengrocer store in London. I remember him telling me that he used to go to the opera at Covent Garden and he used to read Dickens as it came out weekly in a publication. My mother's father was alive, lived with us until I was about four, I think. I don't really remember anything. My mother's mother had died when she was in school.

Williams: So you grew up in London?

Dutton: And I went to school in London and to college in England.

Williams: What part of London?

Dutton: Chiswick. It's in western London.

Williams: What kind of schools did you go to in England?

Dutton: I went to a school called St. Paul's School. It used to be in central London, but moved to Hammersmith sometime a long time ago.

Williams: That was a private school, in our terms?

Dutton: Right, yes.

Williams: Episcopalian?

Dutton: It was founded by Dean Colet, so it did have some religious background originally, but in its charter it was said to be open to people of all nations and all

denominations. That's a very catholic—maybe catholic's not the right word to use in that sense.

Williams: Small-c.

Dutton: Yes.

Williams: So was there an international student body there that you interacted with?

Dutton: Not international. This was during World War II, and there were a lot of refugees from Europe had fled Germany and were living in London, and actually we were evacuated during the war and a lot of them, their parents were under house arrest. My father used to drive several of them back to London to see their parents, since the parents couldn't come and see them.

Williams: Where were you evacuated to?

Dutton: Originally we were evacuated to a big country estate at a place called Magnum [phonetic] on the River Thames about twenty-five miles west of London. Then after the blitz was over, they returned back in to London. So we were not in the actual school building because it was taken over by Allied forces. The Supreme Headquarters of the Allied Expeditionary Forces were there.

Williams: In St. Paul's?

Dutton: Yes. We were in a building that overlooked them, and we could see the generals coming and going during the period before the invasion of Europe.

Williams: Did your family home suffer any damage during the war?

Dutton: My parents sold the house that we lived in before the war, and the house we lived in when we came back, it suffered some minor damage, some windows blown out and some tiles off, but not serious damage.

Williams: That was a formative period in your life. What effect did WWII have on you?

Dutton: Well, it certainly made my schooling a little erratic, moving around from one school to another. I think children are not particularly—they don't really see the real gravity of things, and so the stress didn't really affect me as I'm sure it did my parents.

Williams: So you must have distinguished yourself in grammar school in order to go to Cambridge.

Dutton: Yes. At that time in England there were scholarships. I had a Middlesex County scholarship that paid for my tuition and part of my support at Cambridge.

Williams: Did you go there determined to go into biochemistry, or did you come to that there?

Dutton: No, I had already decided that's what I wanted to do. I remember actually the moment when I decided. I was traveling on top of a double-decker bus and I'd been reading some things and suddenly decided that this is what I wanted to do, to understand the nature of the chemistry of life.

Williams: That must have been quite an "aha" moment for you.

Dutton: It was, actually. I was planning to be an architect before that, and I'm not quite sure how I switched my interest, but it definitely was a definite moment of decision.

Williams: What led up to that? You say some reading, is that it?

Dutton: Yes. I had read a lot of things. I don't remember exactly what I read, but I remember that I was very interested in science topics of one sort or another, astronomy and psychology. I just don't remember how I came to focus particularly on biochemistry.

Williams: Where were you traveling to on the bus?

Dutton: I was somewhere near home. I'm not exactly sure where. [laughs]

Williams: I didn't expect you to remember that detail, but sometimes those memories . . .

Dutton: It wasn't "zing" sort of moment.

Williams: Right. So what was your experience like, undergraduate at Cambridge?

Dutton: A lot of hard work. I remember thinking afterwards that I hadn't relaxed and enjoyed as much of it as I should have done. It was very competitive at that time, very competitive to get in, and then very competitive to get into the majors, and so I needed to study. I studied enough, anyway, yes.

Williams: Did you fall under the influence of any particular professors there?

Dutton: I did. The chair of the microbiology part of biochemistry was a guy called Ernest Gale, and he was sort of impressive. He was working on how protein synthesis was achieved.

Williams: So your experience at Cambridge didn't call into question your decision on the bus.

Dutton: No, no, it absolutely reinforced it. I got completely immersed in it.

Williams: So what was your graduate time like?

Dutton: Well, at that time, the people at Cambridge used to take the top people of their class in the finals, put them in the graduate program, and I think I was number three, which was just outside it, so I didn't get to go to Cambridge, but I went to London. I often think that those were very different days, because I remember going to see Gale, and he said, "I thought you'd do better, but I've fixed you up with somebody in London." So that was it. That's how I came to go to graduate school in London.

Williams: So that's where you did your M.A. and then Ph.D.?

Dutton: Ph.D., yes, in London.

Williams: You received your Ph.D. in '55.

Dutton: Yes.

Williams: Was that fast track or—

Dutton: No. I'm not sure if it's still like that, but in England at that time you were expected to do it in three years, and that was it, partly because there was very little coursework associated with it, so you went straight into research, and the scope of the thesis was probably a little more limited than currently in the States now.

Williams: What was your focus?

Dutton: It was the production of biologically labeled, radiolabeled compounds, and the guy I worked for, Dalglish, was interested in tryptophan metabolism, so he wanted to have some C14 labeled tryptophan, and so that was my main task, which I did. Then I worked for a year or two, continuing in his lab using the radiolabeled compounds, so like a metabolic pathways. Tryptophan gives rise to 5-Hydroxytryptophan and 5-Hydroxytryptamine. This was a pharmacologically active compound.

Williams: So you were working on what we might call an investigative tool, in a way, is that correct?

Dutton: Yes, yes. Mainly what I did was to make equipment. At that time, we had a very limited budget, and a lot of things that you take for granted now were not really available, so I made apparatus. I made fraction collectors and the apparatus for doing the photosynthesis part of the synthesis. I grew *Chlorella*, the green algae, and I made an apparatus for growing it, and it was very efficient in converting carbon dioxide into protein.

Williams: Did you do a thesis then?

Dutton: Yes.

Williams: In that area?

Dutton: Yes.

Williams: That's interesting. Talk for a moment—this is a little bit of a tangent—about the relationship between scientific research and the technical side of things. How dependent has the history of immunology, for example, been on technical development?

Dutton: Yes, I think there is a very close interaction in both directions. Technological advances completely revolutionize areas of research. I mean, flow cytometry is the most striking of them. I remember when it was initially developed thinking there really wasn't much point in it because you could do separations in other ways, but now it's something you use all the time. There's no experiment that we do could be done without hours and hours of flow cytometry. It's gotten so sophisticated that it's absolutely indispensable.

Williams: So that's what I was sort of expecting you to say, that there is an indispensable relationship between the two.

Dutton: Yes. That, of course, was developed by an immunologist. Actually, I think original flow cytometry was analyzing pollen grains, and I don't know how he came to know about this and use it for separating cells. Then, of course, the fluorescent labeled antibodies which actually Susan Swain was in the lab of Albert Coons, who developed that technology. She was a graduate student.

Williams: So after completing your time at London, you then made this trip to America, and kind of interesting how that came about. I read about that, so tell us.

Dutton: Well, it was totally an accident, actually. I had arranged to go and do a postdoctoral fellowship at NIH [National Institute of Health] with a guy called Sydney Udenfriend, and that was in biochemistry on tryptophan metabolism. But for some reason, he decided that he was going to come to England and do a sabbatical in London, I think, so that fell through, and that was a bit of a shock.

But at that time, an American immunologist just happened to come into the lab and say that he was looking for somebody to come and work in his lab, and since I just wanted to go to America and didn't really care what I did, I said, "Okay, I'll come." Actually, it was a little bit more sophisticated than that. I did look into his credibility and found that he was a well-respected guy, and turned out it was a very good thing, because he turned out to be an absolutely wonderful mentor, a

guy called John Vaughan. He died about ten years ago, I think. But he was an excellent person to start off in immunology.

Williams: You intended then to find a way to come to the States in . . .

Dutton: Yes, at that time everybody aspired to do a year's postdoctoral fellowship, and so I came intending to come for a year, but actually the year stretched on to almost three years, and I did go back to England for about a two-and-a-half-year period before finally emigrating.

Williams: What was the allure of the States in '57?

Dutton: Well, I think it was where there were a lot of active research going on, at this place where there was money to do research, and also I just wanted to come visit America. [laughs] It was sort of an adventure.

Williams: So what was Vaughan's operation like?

Dutton: Well, at that time, he was, I think, an assistant or associate professor at the Medical College of Virginia. He had studied with Elvin Kabat, also a leading immunologist, and he had a lab with about five or six people in it, I think, in Richmond. About a year after I went there, he moved to University of Rochester, New York, and we went there. My former wife and I went there and we both worked in his lab.

Williams: Speak about your former wife just for a moment. She also was a scientist.

Dutton: Yes. We worked together while we were in America, and then when we returned to America, to San Diego, by that time we had small children, but she went back to work and worked in Jon Singer's lab at the University of San Diego.

Williams: So, that's right, you went back to London from '59 to '62. What caused that to happen? What were you doing then?

Dutton: Well, originally I had intended to emigrate, so I was going back home and I worked there. I had an NIH grant, very modest by current standards, but it was perfectly adequate to fund me and my little group of people, about four or five people. But I didn't have any position; I just had space. They just gave me space, so that was it. It was clear that getting any sort of permanent position in London was going to be very difficult.

At that time, I had done some work that was attracting some attention, and I got an offer to go to Scripps Clinic in La Jolla. Frank Dixon was the director of the Pathology Department there, and he asked me would I be interested in joining their group, and it occurred to me that since I didn't have any other job, that might be a good idea. [laughs]

Williams: Why were things tight at that point in Britain?

Dutton: Well, Britain went through a very bad economic time after the end of the war, and I remember that at the time I made my decision, I think more money was spent on a single horse race than was given to the entire University Research Committee in a year. It was a lot of support, but it wasn't anything like the level of support that there was in America. The expansion of the NIH funding in America was enormous.

Williams: You were able to take NIH funding to England.

Dutton: Yes.

Williams: Is that unusual?

Dutton: I think it may still be true there are overseas NIH grants. There are certainly not very many of them, but at that time there were a number of them. There was some question of whether they would continue the program, and that also figured in my decision that it was possible that that source of funding would dry up.

Williams: Did you take people from Rochester with you? Is that your team?

Dutton: No, no. When I went back to England, I recruited people in England. Then when I moved to La Jolla, I brought two people with me. One was a graduate student who was a postgrad at medical school, and the other one was an Australian woman who was a technician there. So I started out with two people from England.

Williams: Where was the study of immunology in Britain at the time you left?

Dutton: There had been some notable work in immunology. John Marrack, I think, who's Pippa's uncle, had been a famous immunochemist, and there'd been some other immunologists, but it was not a big field at that time.

Williams: What made you decide to go to La Jolla rather than somewhere else in America?

Dutton: Well, it was an excellent group, Frank Dixon and Bill Weigle, Charlie Cochrane, and people there. It was a first-rate group of people in that department. Plus, La Jolla's not a bad place to be.

Williams: So what was your work like there? That was before you moved to San Diego.

Dutton: La Jolla is a suburb of San Diego.

Williams: Yes, yes, I know. I mean the UCSD. You went to Scripps first, is that correct or not?

Dutton: Yes, in La Jolla. So I was there for about six years, I think, before getting a position at UCSD, which had just been started. I think when I first went to La Jolla, there was a field with a couple of horses in it, and then they put the new campus there, which is now absolutely enormous. I was there just last week, and it's mindboggling how huge it is.

Williams: So what kind of work did you do at Scripps?

Dutton: Well, I was looking at lymphocyte activation. That was the work I had done. I'd shown that antigen actually stimulated lymphocytes to proliferate, and that was such an obvious thing now, it's hard to see why it was important at the time, but it was because nobody had found that that was the case.

We continued on those studies. Mainly what I had done was to develop an in vitro culture system for studying it. Before that, people had mainly just injected animals with antigen and then waited a number of days and bled them and looked at antibodies. So you had no idea what went on in between. So once you would get it out into culture and manipulate the cells, things began to move much more rapidly.

Williams: Is this the work you did with Mishell?

Dutton: Yes. So, actually, that was the second part. The first part was stuff I did in London. Well, the first part was really when I first came to America, worked with John Vaughan, we developed a cultural system for looking at antibody formation, but we had started a response in the animal and then took the cells out and continued the response.

Then I used that system to show that not only did the antigen stimulate antibody production, but the antibody-forming cells were dividing. Then I showed that they were actually stimulated to divide by the antigen. So this developed a lymphocyte proliferation assay. What Bob Mishell did was to devise a system in which the whole response could be carried out in vitro. So for many years we worked with that model. I think we just got rid of the last of the special equipment the last time I moved.

Williams: What were the circumstances for you to move over to UCSD?

Dutton: It was just a good opportunity. A whole new campus was being developed, and UCSD was a remarkable place. They recruited people from all over the States and set up a very ambitious set of departments. They had a global Biology Department that encompassed everything, all aspects of biology from virology, population biology, genetics, and metabolism. They also started the medical

school there, so I was in on the planning of the lower division, the first-year medical school courses. That did open the year that I went there in 1968.

Williams: So pedagogy sort of had an appeal to you, is that right, teaching and—

Dutton: Yes, I do enjoy teaching. It's a mixed blessing. It's a lot of work, especially grading exams. That's not a good part of it.

Williams: But you were still encouraged to continue your research at—

Dutton: Oh, yes. There was quite a lot of teaching that went on at UCSD, the undergraduate courses and medical school courses, but my primary activity was always research.

Williams: Was there continuity between what you were doing at Scripps to what you were doing there?

Dutton: Yes. Yes, and the people who were working with me at Scripps all moved to UCSD.

Williams: What happened to Scripps?

Dutton: Well, they had plenty of people there left.

Williams: I mean, their reputation certainly has remained, hasn't it?

Dutton: Yes. Oh, yes. I think most people, when they move, they like to take with them as many people in their group as they can. Otherwise, things tend to fall apart.

Williams: So talk about some of the highlights of your time at UCSD.

Dutton: Well, there were a lot of exciting things that happened. There were a lot of civil rights demonstrations, a lot of anti-war protests in the early days there, and then there was the development of a third college that was in response to the needs to develop minority student education. So a group of us put together a special program for the students, biology and third college. It was a time when a lot of idealism and a lot of effort put into these areas of education.

Williams: So you were on committees and whatnot to address these issues, is that correct?

Dutton: Yes. The third college had a committee of a number of faculty, a number of students. A number of the minority students were on the committee planning these things.

Williams: Describe the third college a little bit.

Dutton: Well, I can't remember the exact details, but I think it was not specifically restricted to minority students, but I think that probably about 50 percent of the students were minority students. The idea was to have courses that would connect to the student's high school education, which was, in general, less advanced than the main population.

It worked pretty well, I think. I remember teaching in it was pretty tough. It was difficult to get some of the students involved in the sort of biology of it, the science of it. But the third college gradually evolved, and I don't know whether it still has any minority bias or whether it's absorbed into the—I mean, the goal was to have it absorbed into the general education system, and I imagine that's probably happened by now.

Williams: So talk about some of the research highlights of your time there.

Dutton: Well, we had developed this in vitro system and, of course, every five years or so something completely revolutionary happens in immunology and, I guess, in other fields, and so one started working on the new things. One of the things that we did early on was to show that T cells, which help B cells make antibody, do it by elaborating factors. We call it the T cell replacing factor. So in 1970, we discovered that you could stimulate the T cells to make a product which would then replace the T cells in giving help, and these were the cytokines that now everybody knows about.

They didn't sort of catch on immediately, because people were worried that they didn't have any antigen specificity, and so other people were describing antigen-specific factors that turned out not really to exist eventually, but they sort of had the limelight. We tried to fractionate and characterize these factors, and we didn't really have the tools at that time. We didn't realize that we were not talking about a single factor but maybe twenty different factors, and we didn't have clean assay systems to really separate them and purify them. We did eventually. We did purify something that at that time was called B cell growth factor 2, which turned out to be Interleukin 5, and we did actually get the N-terminal sequence of that after purifying it, but we were beaten to the post by somebody who cloned the gene for it, so we decided we couldn't really compete with large groups that had the resources that we didn't have.

So we also worked on MHC, reactions to MHC, histocompatibility reactions which showed that the histocompatibility locus in mouse was the H2 locus. We [unclear] the mixed lymphocyte response to histocompatibility mapped to H2. We did a number of other things with T cells. I remember John Kappler and Pippa Marrack were in their lab. They worked on assays for measuring T cell help and also limiting dilution assays to identify individual helper cells.

Then mainly we went off into looking at subsets of T cells. First of all, there weren't any T cells, there were just lymphocytes, and then first there were T cells

and B cells, and then the T cells were separated into two different sorts, CD4s and CD8s, and then there were different subsets of CD4s and CD8s. So as the years went by, things got more and more complicated and more and more things to look at. Then in more recent years, we've gone into looking at the response to infectious diseases, so we've been working on influenza for ten years or so now, more than that, actually.

Williams: Where did Dr. Swain come into your life?

Dutton: She came to the lab as a postdoc in 1974, I think, yes.

Williams: And she worked a postdoc for you?

Dutton: Yes. Then she became a research faculty member and finally a regular faculty member there.

Williams: And somewhere along the line, she became your wife.

Dutton: Yes.

Williams: Any more to say about your time on the West Coast?

Dutton: It was certainly a very enjoyable period of my life. We had all sorts of exciting things going on in the lab, and I thought for a long time that I would never dream of leaving such a nice place to live, but when we did leave, we went to the exact opposite. We got the farthest place away from San Diego that we could go to and the coldest place and the most empty place. Saranac Lake is in the middle of a very large state park, which is a wilderness area. So it was a very striking contrast.

Williams: Just before we leave the warmth of the West Coast, talk about the group that you worked with there, sort of what was the degree of collegiality and—

Dutton: Well, we were in the Biology Department, and the Biology Department, in its early days, probably its first twenty years, was a group of people who decided almost everything by consensus. It was, I think, a rare example of academic harmony, and so as it grew bigger, eventually it began to split into subsets, but for a long while it was a very, very pleasant place in which relationships in the department were extremely cordial. In our own lab, we also had a great time. We took trips out to the desert together and trips up into the Sierras, and it was a very, very nice place to work, very nice group of people to work with.

Williams: So what were you and your wife thinking when you decided to move to Saranac Lake?

Dutton: Well, she was offered a very exciting position as being the director at Trudeau [Institute], and we'd always had this sort of fantasy that it would be nice to have a little research group office of our own, where we didn't have to deal with any bureaucracy, we didn't have to teach three hundred undergraduates immunology and so forth. We were a little worried about how viable an independent research institute would be, but we decided to give it a go, and actually it turned out to be very good choice, I think. We had an excellent time there.

Williams: Did you visit before—you certainly visited before you accepted the position.

Dutton: Yes. Susie got the invitation, and we said, "Do we want to go or not?" So we said, "If we don't go take a look at it, that's the end of it, so we'd better go and do that." We went there and were much more attracted to it than we expected we would be, so we went back a second time and decided that we really wanted to go.

Then, of course, we had to persuade our group to go with us. I remember we came back and said, "If we decide to go to Trudeau, who's going to come with us?"

They all said, "No. Why would we leave San Diego?" [laughs]

So we sort of shelved the idea for a little while, but then we thought we really did want to go, so we went back a second time and said, "We *are* going. Who's going to go with us?" And everybody said yes. Not everybody. Two of the senior people who were about to move on anyway stayed in La Jolla. They're still there now. They've done very well. But I think about fourteen people decided to move, and I remember a very interesting thing where we were all found in the store buying winter equipment, big jackets and snowshoes and things in San Diego before we went.

Williams: What time of year did you make these two preliminary visits?

Dutton: I think the first one was in April, and I think we went back in August. April, there was still snow on the ground, and August, I think it was raining. But it's a very, very beautiful place. It's spectacularly beautiful, mountains, lakes, and forests and things.

Williams: So did you have any responsibility in providing accommodation for the people that were coming with you, or was it sort of everyone on their own?

Dutton: No, we moved everybody. We had funds to move them. Then one of the things about Trudeau is that they have housing for faculty and housing for postdocs. It's in a small village, and so there really isn't enough appropriate accommodation. So I think we had something like twenty postdoc housing units and six faculty, so new faculty we recruited, and they would live in faculty housing for two or three years while they got settled and decided where they wanted to live. We also had a

daycare center, too, which one of the trustees gave money to fund, which made it a very attractive place for young postdoc couples to come to.

Williams: You and Dr. Swain were having a family, too, right?

Dutton: Yes, they were born in San Diego, but I think our son was sixteen when we came, and our daughter was nine.

Williams: Describe what the Institute was like when you got there.

Dutton: Well, it was relatively small. I think there were about five or six faculty, and it had a relatively modest budget, but I think we were fortunate in our timing. That was the period when NIH funding was expanding, doubling, over a five-year period of 1996 to 2002, and we were able to recruit a number of really excellent people. So the place expanded enormously while we were there. I think we doubled the number of faculty and probably increased the funding of the place about fivefold. So it was a very, very good period. Also we were able to build a new wing to the Institute, and they really were exciting times.

Williams: Did you come in with sort of plan of action, or did it evolve once you were there?

Dutton: We did some pretty careful planning before we moved and then we did continuously planning. The chair of the Board of Trustees, about a year after we were there, asked us to develop a five-year plan for the expansion of the place, and we did that. Then we had a second five-year plan when that was done.

Williams: It sounds very Soviet.

Dutton: [laughs] It was a lot of fun. It's very difficult to do that sort of planning because there's a worst-case scenario and a best-case scenario, and an awful lot of difference between the two, so we would sort of narrow them down to something in the middle and plan around those expectations.

Williams: And they pretty much worked?

Dutton: Yes, they did. Actually, they worked very well.

Williams: So what were some of the major accomplishments that were made by the Trudeau Institute while you were there?

Dutton: Well, I think we worked on a number of disease models, infectious diseases, studied in mice. Mice are so useful because they're genetically manipulatable and they have short lifespan and there's a huge amount of reagents available to use to study immune response in mice. Also, of course, you can do things to mice that you can't do to humans.

So we worked on tuberculosis, on some other bacterial diseases, influenza, toxoplasma gondii, and a worm disease, helig— [laughs]. I can say it if I don't think about it. I'm completely blocked on it. It's a worm that infects the intestine. All of these different infectious agents require quite different types of immune response to deal with them. Some of them require antibodies, blocking antibodies, some of them require cytolytic T cells to kill them, and some of them require cytokine responses and innate responses. Heligmosomoides polygyrus.

Williams: Are describing what you and Dr. Swain were doing or the whole group?

Dutton: We had two or three groups that worked on viral diseases, one very successful group that worked on tuberculosis, Andrea Cooper and her group, and they made some good advances. Also, the previous director, Dr. North, Robert North, he had also worked on tuberculosis and made some very interesting observations.

Williams: Did he continue to work with you all or not?

Dutton: When he resigned, he retired from the directorship, he continued to work, and, in fact, I think he's only just retired a year or two ago, and I think he still has a connection. He lives there at Saranac Lake.

Williams: So were there downsides to your coming there or problems that you confronted?

Dutton: No. I mean, some people, I think, found it very remote. It was fifty miles to the nearest shopping mall, but that didn't worry me. [laughs] Actually, travel in and out was a problem sometimes. You had to drive a couple of hours to the nearest airport unless you wanted to take the little tiny plane that flew into Boston. Of course, the winters were very severe, but, again, I liked that. On the whole, I'd say there was very little downside.

Williams: What about within the Institute itself? Were there obstacles that you encountered or difficult patches?

Dutton: Well, I think the obstacle that is there now is that so much of its funding came from NIH grants. About 85 percent of the funding comes from NIH grants, and they, of course, pay indirect costs on the grounds which run the basics of the Institute. With the pay line now being so low, it's very difficult to keep that money flowing into the Institute, and raising other sources, we have no alumni, we have no patients, and so we don't have the usual sorts of private support that other places have. Plus, we're not connected to any university. There are a number of independent research institutes that are grafted onto universities, but we were completely freestanding.

But it had several very good advantages. It was a small place with only about 150, 200 people, so it was a pretty close-knit community, and everybody got along very well with everybody. Since there were so few people, there was very

little administrative bureaucracy, so one can certainly contrast it with a big state university. It was always a [unclear] simpler to get things done.

Williams: You had a board, is that correct?

Dutton: Yes, we had a Board of Trustees who were responsible for the fiscal integrity of the place and had some oversight of the scientific policies, but we also had a Board of Scientific Advisors, because the Board of Trustees were mostly laypeople who did not have any real scientific knowledge.

Williams: Were they local, or did they come from all over?

Dutton: A lot of them were a legacy of the fact that the Trudeau Institute had previously been a sanatorium, and a lot of them were wealthy people who had country houses or even country estates in the Adirondacks. We did also have some scientists. We had Ralph Steinman, who recently died, a Nobel laureate; and also Charlie Janeway, who was also on the board; and one or two other people, Vince Fischetti. They were very useful in that they bridged the gap between the lay trustees and the scientists at the Institute.

Williams: And they were there before you got there?

Dutton: Yes. Charlie Janeway, I think, Susie recruited to the board, but Ralph Steinman had been there many years previously.

Williams: So what were the reasons why you left?

Dutton: Well, partly Susie was no longer director, and we also were very attracted to the group here at UMass, some very good virologists who we interact with and also a number of the other people in the Pathology Department, and then there are groups in other departments that we now interact with. Also we're sort of nearing retirement time, and we have a very nice house on Cape Cod that we can visit more conveniently from here. So it seemed like it was time to move on, and hopefully this is our last place. We don't plan to move again.

Williams: Have you been back to the Institute lately?

Dutton: We were there a couple of weeks ago. There was a memorial lecture for Ralph Steinman, and Susie gave the introductions.

Williams: How did things strike you there now?

Dutton: Well, they're obviously hanging in there. There are some very good people still there, and hopefully they'll be able to get some funding that will allow them to continue.

- Williams:** So talk a little bit more about this place. You said that they're a good group of people and so forth. Is there any particular mission of the department here that you see?
- Dutton:** Well, I think the state, when they decided to put the medical school in Worcester, put a lot of money behind it, and I think UMass-Worcester has sort of been steadily rising in its academic profile. I think it's beginning to establish a very strong reputation, and, of course, the new building that they're putting up just across the way here will allow them to continue that. Getting research funding is very difficult for everybody, but so far people are managing to get at least some level of grant support.
- Williams:** Do you have much connection with the academic program?
- Dutton:** I personally don't, no. I do give a few sort of seminar-type meetings with the students, but I don't do any of the mainstream teaching.
- Williams:** I was looking at a description of the reasons why the medical school was founded, and one of them was a state commitment to the production of more primary-care physicians. Is that still part of the mission here?
- Dutton:** Yes, I think so, and I think they continue to be rated very highly in that area. I forget what it is, but they're right up in the single-digits listing in the country.
- Williams:** Are there other areas of particular focus?
- Dutton:** Well, they have Craig Mello, who's a Nobel laureate for his work on microRNAs, and they have a very strong group in innate immunology, and I'm sure they have groups in other areas of medicine that I'm not familiar with, but certainly in the area that I'm familiar with, they have a very good reputation.
- Williams:** Looking back on your scientific career, what do you want to be remembered for?
- Dutton:** Well, I think my main contribution was to develop in vitro models for studying the mechanisms of the immune response, using those for discovering that there were these cytokines that were involved in the interactions between different types of lymphocytes. That's probably my more important things.
- Williams:** To the layman, what importance does that work have?
- Dutton:** Well, it's mainly understanding how the whole system works. We haven't, for the most part, focused on any translational research. I think that when I first started out in science, the operation was very much smaller than it is today. I think I did a calculation the other day that there are probably twenty times as many people doing immunology now as there were fifty years ago, and the amount of funding devoted to it was also twenty times smaller. So for people to

sort of follow their idle curiosity just understanding how biological systems work would seem to be reasonable now. I think with more investment of public money, there's more of a compulsion to have some socially important goal, and so the focus of research has shifted more to things with some obvious translational application. And I think that's obviously good, and I think it was the basic inquiry not targeted at anything in particular that was very important in making major discoveries, and I think we've lost that a bit, because you can't get funding for finding out some esoteric question if there's no obvious application.

Williams: Have you maintained contacts with and awareness of what's going on in Great Britain?

Dutton: Not a great deal. Part of the reason is that I left England as a biochemist, and all my biochemistry colleagues continued to do biochemistry. whereas I did immunology, so I haven't really had much scientific contact. I know some of the people, obviously, but—

Williams: I guess I'm curious to know. contrasting immunology in this country and there, do you have any thoughts about that?

Dutton: I remember you asked me earlier about British immunology, and I realized I totally overlooked Peter Medawar, a Nobel laureate who was an outstanding immunologist. He was a transplantation biologist who also won a Nobel Prize. The big immunology group is Mill Hill, the Medical Research Council, and I've certainly interacted with Ita Askonas, who was the director of the virology group there for many years, because she also works on influenza. A number of my colleagues here have also come from Britain, Michael Bevan and half a dozen or so very close friends.

Williams: You were also part of the very famous brain drain, weren't you?

Dutton: Yes. [laughs] There really wasn't a great deal of immunology research at the time I left. A big group at Birmingham has been for many years, but I don't know that they were—I guess they were functioning when I left. A guy called Philip Gell was at Birmingham, and there's still a good group there. Also there is a group at Imperial College in London, so there are some outstanding groups there.

Williams: Do you think the States still has the same kind of allure that it had in the fifties when you wanted to come here?

Dutton: It does in the sense that a lot of very good research is being done. I think it's very daunting for young investigators when one looks at people who are graduate students and postdocs, thinking that they've got to put in grants. In order to be viable, they need two basic NIH grants to even run a modest operation, and with the pay line being less than 10 percent, I don't think all of them are going to make it. It's never quite clear to me where people who don't go on in academic

research go to. Obviously they go into biotechnology of one sort or another. But the old model where you studied under your professor, then you became a professor yourself isn't going to work, because you had a rate of expansion that was too great to support.

There was a paper in *Science* that I keep trying to find that I've never been able to retrieve by somebody called Carter, who pointed out that the rate of expansion of the NIH budget for science would exceed the gross national product by the year something or other in the future, that it was just rising at an unsustainably fast rate. Of course, that's the financial, cultural environment we've lived in for the last fifty years. We've always had that extra money growing faster than everything else to keep the operation rolling, and then 'round about 2003 that stopped. So the current problem is inevitable. It's not something that could have been avoided by keeping on expanding, keeping on expanding.

I think it may require some changes in the structure of the way academia is run, sort of entrepreneurial way that it's done at the moment in that the scientist himself is responsible for raising his own research money. It introduces too much uncertainty into people's careers. If you really can't say whether you'll have enough money to fund a couple of graduate students two years from now, how can you responsibly take them into your lab? Some sort of more stable type of funding that they have in European countries, I think, is something that we're going to have to go to, although many people feel that that's a regressive step. They feel that the investigator-initiated research is what made American research so successful.

Williams: Talk a little bit about the European model and how it's different.

Dutton: Well, I think that government money goes to universities and departments, and then the departments hire people and they fund them to considerable extent. There are, of course, grants, but it's a sort of two-stage thing. There's secure money and then there's money that's applied for. So there's a more stable base for people who are in research. It leads to a more hierarchical structure that ideally, if you could always stay with the entrepreneurial one, that would be better, but if that doesn't work, you have to do something different.

Williams: You mentioned a moment ago that you really have to have two grants in order to succeed as an investigator. Explain why that is so.

Dutton: Well, the standard sort of grant is \$250,000, and if it's got to pay half of the faculty salary and all of a postdoc salary, that'll pay about half a faculty salary, one postdoc, one technician, and the money required for them to do their research. You need the second grant to pay the other half of your salary, another postdoc, and another technician. So if you don't have a group of about four to five people, it's very difficult to be competitive. If you've got to compete with a big group

that has lots of people, you'll lose out, and if you're not competitive, you won't get your next grant. So I think it tends to be sort of a winner-take-all situation.

Williams: So how does that work in the application process? You apply for the first grant and then immediately once you get it go for the second?

Dutton: Junior faculty when they're recruited, they generally get a startup package that is designed to set up their lab with equipment and then fund them till they can acquire their own funding. So at Trudeau, we had an amount of money that was calculated to fund them for three to five years, by which time they had to be independently viable, and that, by and large, is what happened, but it means you have to only recruit people who are going to be really successful, otherwise you've wasted your startup package.

Williams: And the funds for the startup package come from NIH?

Dutton: Well, at Trudeau they came from the interest on the endowment, and we used to have about \$2 million a year in sort of discretionary research-funding money, which we used for startup packages and for supplementing people who were temporarily between grants.

Williams: And where did those funds come from?

Dutton: They partly came from the overheads for the grants. The grants had an 84 percent overhead, I think, at Trudeau, and they also came from various other funding sources, a few funds from the state, and also we had an earmark both from the state and from the federal government. They were put into an aggregate pool. They weren't specifically—I mean, we didn't take the money from one thing and use it for something else, but they just contributed to the general operation of the Institute.

Williams: Did you enjoy any particular support from the state because you were a treasurer?

Dutton: Yes. I think the Institute, it's such a small community that the sort of financial viability of the community was dependent upon having a functioning institute, so local senators and representatives would work to get state funding of one sort or another. Either you support the Institute and keep the community viable or you let the Institute go and then you have a community that needs to be supported. So it's same amount of money, whichever way you distribute it.

Williams: So the Institute was critical to the economy of the community.

Dutton: Yes. The community had a hospital, a regional hospital. It had the state prisons, a lot of state prisons in the Adirondacks, correctional facilities. It had Trudeau Institute, had a community college, and American Management Association, and tourism. So those are the main incomes of the community.

Williams: Let's turn to talking about the American Institute of Immunologists. You became a member in 1963, which was—

Dutton: I did? Yes. [laughs]

Williams: Well, yes. That's just about at the time you arrived in La Jolla.

Dutton: Right.

Williams: By the way, when did you become an American citizen, if you did?

Dutton: 1968.

Williams: So you really did burn your bridges. [laughter] You became in '70, '71, the chair of a Course Planning and Faculty Committee for the AAI. What was that about?

Dutton: Wasn't that the summer teaching course? Yes. The AAI holds annual courses at either the introductory or advanced level. I think at that time it was just one level. We ran the course at UCSD, and I think I ran it a couple of years. So, a two-week course with maybe ten, twelve faculty giving lectures, and they've generally been run on campuses in the summer months when they're empty.

Williams: And the target audience there was?

Dutton: They would be beginning postdocs, maybe graduate students who would come and get a sort of overview of current immunology research.

Williams: That's the advanced course, or was it that course at that time?

Dutton: I think at the time I ran it, there was only one course then. When we split it into two courses, I don't remember. Sometime after that, I think.

Williams: Then in 1990 you joined the Council.

Dutton: Right.

Williams: How did that make you feel?

Dutton: Well, that was good. It was interesting to meet twice a year and see what was going on in the field. I'm not sure that I quite realized what I was letting myself in for when I agreed to stand for election, but it was a good thing to have. It was pretty pleasant meeting with colleagues and discussing the various issues and juggling the financial problems of the society, planning the meetings, running the journal and so forth.

Williams: Were there any particular hot-button issues while you were on the Council?

Dutton: I remember the year I became president, there were some financial problems with the operation of the journal, so that was something that we had to deal with. But there was always the issue of whether the meetings would be financially successful. If something drastic happened in the world and nobody came to the meeting, then you'd be out several hundred thousand dollars, or if the exhibitors didn't turn up because they thought the meeting wasn't going to be big enough. So there were all these issues.

I think the biggest issue, though, was the worry about the level of NIH funding, not so much initially that it was declining, but it was no longer expanding as it had been. Then later on, in the last five years or so, it's actually been declining, so a lot more attention was taken to public affairs and talking to congressmen and senators.

Williams: What was the issue with the journal?

Dutton: I think it just wasn't being run very effectively and not enough attention being paid to revenue streams and having it published and so forth.

Williams: Do you recall what corrective actions you took?

Dutton: I don't know that I took corrective actions, but the executive staff at the AAI Office did, and they made sure that there was good advertising revenue.

Williams: I read your presidential message in which you talked about the funding matter and then challenged the organization to come up with ways to get the message out to the general public and to politicians and whatnot on the importance of the work.

Dutton: Right.

Williams: Did it have legs?

Dutton: Well, it's very difficult. I mean, the connection between an experiment that somebody does and then ten years later the applications, it's very hard to trace, and it's very hard to describe it in terms that the lay public will understand. The best examples are things like discovery of monoclonal antibodies that have lots of technical uses and also some clinical uses they used in therapy, but it's not something that's immediately understandable to somebody without any basic biology or medical language. We did manage to put together a number of stories which were distributed, and what impact they had, I just don't know.

Williams: Did you make visits to Capitol Hill while you were president?

- Dutton:** I did. I went on several, talked to my local congressman. I remember meeting with the congressman from Rochester, New York, and also with the staff of the two senators from California, Dianne Feinstein, and meeting with those people. Mainly one meets with their staff who are in their mid to late twenties and extremely enthusiastic and extremely knowledgeable. We had a very good public affairs fellow at the time at the AAI.
- Williams:** Patrick White?
- Dutton:** Bob White, I think his name was. [ed. Patrick White was the director of AAI public affairs]
- Williams:** Yes, Bob White. That's right. I just read Gail Bishop's current presidential message saying exactly the same things that you did.
- Dutton:** I think all the last ten to twelve of those said the same thing.
- Williams:** That's right. There's been no significant breakthrough, has there?
- Dutton:** Well, I think the trouble is that most of the people in basic research are applying for these RO1 grants, and not only has the total amount of money available stabilized or even declined a little, but there's been a shift towards more translational programs. So a lot of the money that was going into what I would consider to be basic research is now going into translational programs of one sort or another that pay for things that are not research. So the amount of money for research has dropped rather more than just a look at the total budget would suggest. Now, as a basic researcher, I would say that it would be nice if the translational part was paid for out of another pot, but that doesn't seem to be the going idea.
- Williams:** Where does immunology stand compared with other scientific branches that NIH funds?
- Dutton:** I actually don't know. I suspect they're fairly comparable. There have been special initiatives like money put into HIV/AIDS research and things like that, but on the whole, I think it's been reasonably stable. Probably more money has gone to diabetes research and so forth, but, actually, I don't really know.
- Williams:** You received the Lifetime Achievement Award from the AAI in 2004. How did that make you feel?
- Dutton:** Good. It was nice.
- Williams:** You're a fellow of the American Association for the Advancement of Science, and that's quite an honor, isn't it?

Dutton: Yes, certainly felt good.

Williams: Was there any particular reason why you were nominated and elected to that?

Dutton: No, I think that some people noticed that I wasn't a member and thought I should be.

Williams: Another position you held with the AAI was as representative to the international body. What was that like?

Dutton: The international body has its own president and so forth, but then there are people sort of who are in liaison to it. It's not a particularly time-consuming activity. It's just a question of choosing the next country that will have the triennial meeting. I remember the year that I was president, it was in San Francisco, and I think Pippa Marrack was the Madame Secretary of the International Congress. We had a very nice meeting there.

Williams: What is the international body like?

Dutton: Well, it has a large membership. I'm not sure how many countries there are. Every three years we have a meeting. The first one was in Washington, D.C., in 1970 or '71, I can't remember, and then we've had them in Japan, Canada, Australia, Sweden, France, Germany. The one this coming year in '13 is in Italy. Had them in Budapest.

Williams: What goes on at the meetings? Is there a sense of mission there in particular?

Dutton: They are just a very large meeting, covers really very similar set of topics to the AAI meetings. It's an opportunity to meet people who you don't otherwise normally get to see at meetings. They are very exhausting because there are multiple sessions going on simultaneously, so one can only sample small amounts of it. I've enjoyed going to a dozen or so of them. Had them in India, Brazil.

Williams: So with the financial difficulties we're having here, do you see a reverse brain drain occurring, and is that likely to occur?

Dutton: I just met somebody the other day who's going to take up a position in Singapore, leaving from California. I don't think it's happening yet. Certainly some Asian countries are beginning to invest heavily in research. But how much of that's going to be in immunology rather than in technology and things, I think it's not an immediate issue.

Williams: Looking back over your career, do you have some particularly happy moments?

Dutton: Yes, I think the most exciting things are in the lab you get an idea of how something works, and you test it and you find that that's the way it works. That's

the most exciting thing, to do an experiment and find that your idea was correct and to be able to prove it.

Williams: Did you develop a particular modus operandi for doing your scientific work?

Dutton: I think one thing that I tried to do was to make sure that everybody felt that they could contribute to what was going on, so in the lab we always took the view that anybody should come forth and say whatever they thought they wanted to say and not feel that they had to keep their mouth shut, and I think that's always a very fruitful way to operate. You find that people who you least expect to say something important actually quite often do. The more input you get and the more involvement you get in the research, the better. So I think we had a very egalitarian sort of structure in the lab.

Williams: Would you advise trainees at this point to pursue a career in immunology?

Dutton: I think that you have to be really interested in what you're doing if you're going to be successful, so I think people who feel compelled to do research are the ones that should be going into their career, because otherwise they won't have the motivation to be successful.

Williams: Any particular path you'd suggest to those who are a little bit less motivated?

Dutton: Well, that's their problem, I guess. [laughter] If they want a specific training for some non-research-oriented job, if they have a clear idea of what it is, that's a reasonable thing to do. But I think that most of the successful people that I know are compelled to keep coming back to the things they study. They do things, they get frustrated, they get disappointed, but then they feel they have to go back and try again. You have to have an intensity of feeling to be successful.

Williams: If you had it to do over again, would you pretty much do the same thing?

Dutton: Yes. I think I've been very fortunate to have a very enjoyable career.

Williams: And what does a scientist do for fun?

Dutton: Oh, all sort of things. Depends who they are, I guess. I like outdoor activities. I like reading. I like music, travel. I don't have a particular thing like some people who like to go sailing on their yacht or skiing or things like that.

Williams: You didn't become a downhill skier?

Dutton: I did, but I never was very good at it. I remember struggling on Whiteface up in the Adirondacks, my daughter trying to get me to go on more dangerous slopes. [laughs]

Williams: Are we leaving anything unsaid today that you'd like to express?

Dutton: No, I think we've covered pretty well most things.

Williams: Very good. Thank you very much for this interview.

Dutton: Thank you.

[End of interview]