

Department of Surgery History Interviews
by Dr. James Gifford
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This interview presents Dr. R. Randal Bollinger, Director of the Transplantation Immunology Laboratory, Department of Surgery, Duke University Medical Center. The subject of this interview is Dr. Bollinger's career as a surgeon and his research interests and particularly the work of his laboratory within the structure of the Department of Surgery. This interview takes place in Dr. Bollinger's office, Room 117 Bell Building, DUMC. Dr. James Gifford is the interviewer.

Dr. Bollinger, perhaps we could begin by having you tell us about your background, particularly as it pertains to your career in surgery and your research interests and how you arrived at Duke.

I was a medical student at Tulane University in New Orleans, Louisiana, when the first heart transplants were performed. Also, during that time we had a new faculty member named John McDonald who had trained in part with Bernard Amos in New York before Dr. McDonald came to New Orleans to work on the faculty at Tulane. It was Dr. McDonald who first took me to the operating room and introduced me to transplantation surgery. And therefore, when it came time to find a place in the United States to go for training in surgery with emphasis on immunology and transplantation, I asked Dr. McDonald for his advice and where might be the best places in the country to go.

He knew of a young, rising star, a bright physician from Hopkins named David Sabiston who had taken over the Department of Surgery at Duke University just a couple of years before. In fact, this was 1968-69 when I was talking to Dr. McDonald, and Dr. Sabiston had really only started his tenure at Duke. Dr. McDonald mentioned also that one of his scientific mentors, Bernard Amos, happened to be at Duke as well. And it was during those years that Bernard Amos was defining his ___ compatibility lowcite. Together with Rose Payne and John Dossier was really putting HLA on the map of science.

I came to Duke then to see these two people and interview here with both Dr. Sabiston and to talk with and interview with Dr. Amos. It was clear from that initial exposure in 1969 that there was only one good place for me to come for my training, and that was Duke University. Therefore, in 1970 I came here as one of Dr. Sabiston's interns in surgery. I stayed here for two years after which I went into the Air Force because as you recall this was Viet Nam wartime. Almost every physician who graduated from medical school in the late sixties and early seventies had a military obligation. Mine was to the Air Force, and I left here in 1972 to spend two years at the School of Aerospace

Medicine. I was a flight surgeon who did research then because there were more flight surgeons coming home from Viet Nam than going over. The war in southeast Asia was winding down.

I had the fortunate experience of spending two years in the Air Force doing research before coming back to Duke in Bernard Amos' Immunology Division as a Research Fellow in Surgery and a graduate student in Immunology. And that's how I spent the time from back in the sixties. I got to train with David Sabiston and Bernard Amos.

Let's go back to the first two years you spent at Duke when you were doing your two years of internship and early residency. Can you tell me what your responsibilities were during those two years and what kinds of things you were expected to do and learn and who taught you?

Everybody expected the interns to be able to do everything. In those days we really had to. We drew the blood, there weren't blood draw teams, we started the IV, there weren't IV teams, we assisted in surgery, we took care of patients on the ward on an every-other-night call schedule. We were in the hospital most of the time. We were here literally 36 or more hours and then off 12, and that was how the program was organized. Our teachers were both the professors and more senior residents. In fact you may be interested to know that one of my teachers during one of those early years was Bob Anderson who in just a few days from now is going to become our new Chairman. Bob was my Chief Resident when I was a Junior Resident. I learned a lot from him.

I would say that there were some teachers who were more effective than others. Among the most effective were those who either taught you from their vast experience or they taught you because they befriended you and, in the fatherly way, introduced you to what you should have known. And those were people like Del Stickel who taught me kidney transplantation here.

What kind of research did you do while you were in the Air Force?

I was a "stress physiology research physician." I studied all sorts of stress forces around our pilots and astronauts, by the way. For example, we modeled the Apollo Soyuz mission, the combined US-Russian satellite linkup to make sure that our astronauts wouldn't get the bends when they went to the high-pressure nitrogen environment of the Soviet capsule and then came back into our low-pressure pure oxygen environment. As you can imagine, they were moving from a high-pressure to a low-pressure environment after having had their blood saturated with nitrogen. Just like deep sea diving, but the pressures were different than one would see in deep sea environment, but we had to make certain that no bubbles would form. We used chambers at the Brooks Air Force School of Aerospace Medicine to go through exactly the nitrogen concentration and pressure situation of the Soyuz capsule for a period of time, after which we moved volunteers into

a reproduction of a US internal satellite environment. We then used doppler techniques and examinations to make sure they didn't develop nitro bubbles, and they didn't.

Dr. Bollinger, you returned from the Air Force to take up the career as a Resident at Duke. Can you describe the structure of the Residency and the requirements of the Residency as you experienced them?

Just to clarify first. When I came out of the Air Force, I went into graduate school. I spent the next two and one-half years getting a Ph.D. in Immunology with Bernard Amos and David Scott. So, although I was a Research Fellow and was in the Residency, it was not in the clinical rotations. It was the Winter of 1977 when I first went back onto the wards at Duke Hospital. At that time I had been away from it since 1972. So, it's really like starting over. It was quite a shock for a young immunology Ph.D. to go back into the surgery residency as a Senior Resident. I started with Howard Filston on Pediatric Surgery.

I'll never forget the first operating day. I reported to his operating room and we had this tiny, little patient that was only about a foot and a half long, and it was my job to start an IV on that patient. Oh, my. It was one of the most sobering experiences of my life. It took me roughly about an hour to get some kind of vascular access in this little child so that we could proceed with the operation. And finally it became time to go and scrub, and Dr. Filston indicated that I ought to go scrub first to prep the patient. The last place I had operated on any patient was at Wilford Hall in the Air Force and there all of the scrub sinks were out in the hall, so I walked out into the hall in Duke South to look for the scrub sinks not realizing that they had the scrub sinks off the side of the operating rooms between ORs. There were no scrub sinks in the hall. And I had this horrible, sinking feeling that I didn't even know where to go to scrub at Duke Hospital, and there was no way I was going to finish the Duke Surgery Residency.

I looked in through the little glass window in the door and there was Howard Filston with this perplexed look on his face, just looking at me looking back through the door at him. It was clear that I didn't know where I was supposed to go, and he gave me the little finger point "over here" to the right was where the scrub sink was. So I sheepishly walked out of the hall, back into the OR, past Dr. Filston, to the scrub sinks, and finally got that baby prepped. It must have been an hour and fifteen minutes after I started before I got the baby scrubbed off. That, Dr. Gifford, was my beginning back into the Surgery Residency Program, and it went downhill from there because it was a very demanding residency.

I say "downhill" facetiously. Obviously, I learned a whole lot from that and other experiences, and I was taught by quality people at Duke to take care of very sick patients. But still every other night there was no one in pediatric surgery to cross cover for me so that if something came up on my night off, I would come back and take care of it. We were extremely busy for a two-month period on pediatrics. We saw nearly every congenital anomaly that exists. Even Dr. Filston commented that was one of the most interesting times that he spent at Duke, and I don't think it was because I was his resident.

I think we really saw some unusual patients, including conjoint twins. That's a rather unusual phenomena.

I understand that residents who graduate through the Duke Surgery Program end up doing more operations and such than graduates of most programs. Do you feel that's accurate, and, if so, do you feel it's valuable?

From the counts that I've seen, I'm sure that it's accurate. A lot of our surgery was done in the senior years and chief years. We didn't do as much surgery as interns and junior residents as my colleagues who went to the Charity Hospital in Louisiana. But at the end of ten years of residency which is a period of time in which I was involved in either research or doing clinical work, I had a vast surgical experience. It is key that teachers of surgery would also be themselves excellent surgeons. And I believe firmly in that.

In talking and writing to people who have gone through the program, there is a uniform respect for the standards. There is a minority opinion that says that the standards are awfully hard on human relationships and, particularly, marriages. Is that a fair comment, or are people blaming the residency for weaknesses that would have become apparent in the relationships in any case?

There is no doubt that every-other-night call schedule is a huge test of a relationship. I don't think it is an unfair characterization at all to say it stressed the family more than any other experience that I've had, but I'm still married to the same beautiful redhead and we're planning our 30th wedding anniversary for May 1, 1995. So, I'm in my 30th year of marriage despite the surgery residency, not because of it, but despite it. I'd say that if a relationship was going to flounder, the residency would test it to the point that it would become apparent at that point that it was going to flounder. It may be true in some cases that it caused a relationship to flounder. I can't speak to that, but I do know the relationship could survive the residency. The fact is that being on call every other night, coming home dead tired in many cases, left no time for the family. And that's the test and reason it is a problem.

For those of us involved in the residency, there was little difficulty in that we were so caught up in what we were doing that for 36 or more hours we didn't even notice the time passing. But during that 36 hours our spouses or children or both may have not been so caught up in what they were doing and, therefore, were looking forward to the moment that their spouse came home to share the children, share the adventures of the preceding day and a half, and instead found someone who was so tired they couldn't stay awake to eat dinner. So, they didn't have the companionship they might have wanted during those times. It's a stress, therefore, for the spouse and for the children more than it was for the individual who was involved in the training program. That's my personal view as to why so many of the marriages either made just before residency or during those stressful times didn't make it. It's true that our track record for both husband and

wife finished in the residency wasn't very good for some of those years. When I was a senior resident at the VA Hospital, I was in a room with five other residents discussing life as we took a few moments during our nights on call. I was the only one who was still married out of the group of six of us, all of whom had been married. I think your characterization is accurate. I think that it was a test of relationships, but some relationships that survived it are forever. You will see many, many such marriages that were made strong. By having gone through the residency together, there is nothing, not near disease or untoured events of the future that could put such people asunder after they had survived the Duke Residency together.

Was any formal attempt made to cope with the problem? Were there any resources available to couples under stress that they could avail themselves of if they wanted to?

I don't know if the Department arranged anything. We found through our Church a support group that allowed us to get through the hard times. Our nearest family members were 900 miles away from us in New Orleans. They were certainly not close enough to come at a moment's notice when one had stress or one had a problem. But we found a group of like-minded, very involved, quite supportive people about our age at Duke Memorial Methodist Church and that surrogate family served my family very well during the stressful years. In fact we still go to that same Church and have those same friends.

Switching back now to the time that you finished your training and took up work for the Department of Surgery, was that the date at which your current laboratory began?

Yes. During my Chief Residency year I wrote an NIH grant that was funded. And so, when I started in July of 1980 I had a research grant and could hire a technician and then had a laboratory from the very beginning.

Can you talk about the work that your laboratory has done and is doing, the lines of investigation that you pursue, and why you pursue them, and how that relates to your clinical work?

Transplantation is one of the areas of applied immunology that allows one to have a clinical interest and a research interest that are, in all respects, compatible. There is no schizophrenia between one's research program and one's clinical practice. Every time we do a transplant, there is an element of the unknown and how a particular patient is going to react to the organ. The phenomena that we observe in the clinic are precisely the ones that we study in the laboratory, so that it was easy in this particular area of science to have clinical and basic work that paralleled.

The basic work that I was doing in 1980 would have been regarded as applied research using the standard of 1994. But it was state of the art. It was the best that we had available. That was the pre-molecular era. And so the kind of cellular studies that we were doing on sensitized recipients, on the induction of unresponsiveness, termed immunological tolerance, was the state of the art of immunology at the time. Over the subsequent 14 or 15 years, all of science has become much more molecular and, therefore, some of the research programs that we currently have underway in this laboratory, are at a much more basic level than we started 15 years ago.

The primary areas of research interest in recent years have been cross-species transplantation and small bowel transplantation. The cross-species transplantation has taken off with the addition of Dr. Jeff Platt to our research group. The research group has changed from eight of us, including technicians and residents, up to 38 of us including biochemists and molecular biologists, as well as the cadre of students and residents and research technicians. So we have a much more extensive, in-depth effort now that goes all the way from clinical transplantation down to the most basic study of the molecules involved in xeno reactions. It really is a broader spectrum research effort involving many more people now than it was in 1980 when I started.

Can you speak in a little more detail to the lines of research that you are pursuing at the moment?

Right now we have a program project in the laboratory that is funded by the NIH that is focused on eventually creating suitable animal donors for human recipients. And I say creating because with the work done in transgenic pigs, in conjunction with the DNX Corporation, we're really creating animals that don't exist in the world right now. That type of animal that is more resistant to immune attack when the organs of such animals are placed in human bodies offers the potential for solving the donor shortage which is the limiting factor in organ transplantation today. I would say that although this is at the moment rather basic in its effort the potential application is huge. At the same time, occasional liver transplantations come along who have fulminate failure and have to be maintained in some way until a human organ can be found for them. Some of these patients are undergoing perfusion of xenogeneic, namely porcine, livers in order to keep them going in the interim until they can be transplanted with an allogeneic human organ. So, this type of clinical experiment is not only having some therapeutic benefit for patients but is providing material for the continuing xenografted experiments in the laboratory.

In addition, we have interest in immunosuppressive drugs. There is a revolution in immunosuppression underway. Whereas we've had immuran and prednesone since the early sixties and cyclosporin since 1983, OKT3 since 1985, you see just a handful of drugs to use over the history of modern transplantation. Whereas that has been the case for the first 30 years we now have twice as many new drugs in various stages of trial. We are involved in looking at some of these drugs. Breckquinar and rapimycin are two of

the drugs that we are currently studying. That, in a nutshell, is some of the ongoing research at the moment.

On a couple of occasions you have mentioned Dr. Platt whom I've also interviewed and who also has what's called a laboratory. You speak of your research group as being inclusive of both of you and so I presume of both laboratories. What's the difference between a laboratory and a group?

We've seen an evolution here in our Department of Surgery of how research is to be and will be undertaken. I think it's a healthy evolution that is probably the wave of the future. When I started, each surgeon who was interested in research or who had the capability of undertaking research had his independent, small laboratory. There were about as many laboratories as there were associate and assistant professors of surgery. That type of approach to research was a viable alternative when there were large amounts of research money available and when research done at the level of the whole organism or cells requiring modest expertise in basic science was the level of research throughout the country. As research has become increasingly molecular, as the techniques applied in research have become ever more specialized, as the amount of money available to do applied research has decreased, it's been increasingly necessary for state-of-the-art research to be done with specialists who do nothing else but that work. The model for advance in science is now to have people like Eli Gilboa, Dani Bolognesi, and Jeffrey Platt who spend all of their time thinking about these problems at a molecular level, lead research groups, and provide a place and an opportunity for clinicians to plug their specific interests or applications into that more basic research efforts. That's at least the model that is proving most successful here in our Department at this time. It's a different approach than we had 15 years ago. But I believe it's going to prove to be a more successful approach for the rest of this decade.

It's a conservative approach when it comes to resources, I take it, in that you guys don't duplicate what the other is doing.

Exactly. We have a laboratory of transplantation research that has certain facilities that are quite expensive. When any of us need to utilize those facilities, we take advantage of that and when we are not using them someone else is. That allows a rather expensive and limited resource to be widely used.

Back 20 or 25 minutes ago you spoke about having come to Duke in part because of Dr. Sabiston's presence. Can you say something about Dr. Sabiston's own role in the Department as Chairman and leader?

Dr. Sabiston is a unique individual. There has not been in my experience, or do I expect there ever will be, somebody on the American surgical scene with his ability, charisma, leadership, knowledge, and experience. He has set the tone for this entire

Department. He has set the standard. He's put his stamp on every aspect of what takes place in this Department. He pays attention to every detail of the activity of this Department in a way that I would have thought before I met Dr. Sabiston would be impossible to do. From the student education to the resident education to the faculty development to the clinical care in the operating room, to the outpatient clinics, every aspect of surgery at Duke University has had the stamp of Dr. Sabiston on it.

Things don't happen here unless Dr. Sabiston approves them. When new things are needed, he has been the spark plug to get them done.

You describe a vision in breadth. Where do you think he gets it? Where does he come by his vision?

My knowledge of that is very limited, but my belief is that he is unusually intelligent, that he reads widely, that he has by virtue of his long experience and ability gained entry into both the leadership circles and editorial circles at the very pinnacle of American surgery in a way that he is exposed to new ideas from all over the country and the world. Now some people could be exposed to these new ideas and would be overwhelmed by them. He's able to process these in a way that uses them constructively and builds new programs, not the least of which is his outstanding Department of Surgery. That's my guess as to why it's true. He is a man of superb ability who has read widely and who is now consulted by other surgical leaders throughout the world for his advice.

Dr. Bollinger, I usually end these interviews by asking the person interviewed if they have any question that they think I should have asked that they want to answer.

I guess that the only other aspect of this laboratory that I value very highly is the young people who come through the laboratory. There are some people now like Allen Kirk, our current Chief Resident, who ended up getting a Ph.D. in Immunology. Scott Pruitt is another who is going to be an M.D., Ph.D. who got started in transplantation immunology in the laboratory. His thesis defense is tomorrow. He's finishing his doctorate now. People like Bob Harland, who is a young Assistant Professor on our faculty now and has started his transplantation in this laboratory, Ben Vernon, Allen Kirk, Scott Pruitt, those folks are the future of transplantation surgery in the United States. Stuart Knackty, who is now on the faculty of the University of Wisconsin, began his research here. And I could name others as well. I think having a place for young people to spread their wings, have the freedom to choose a project and then delve into it as deeply as their able, to see them succeed is one of the joys of being on the faculty here at Duke. They are really quality people who have been attracted here by the institution and our leader and being part of their training is one of the joys of staying on the faculty. I guess that's the final comment that I'd make.