Seasons

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First of all, I would like to thank everyone for coming and to thank all the speakers. This really has been a wonderful symposium full of history, new avant-garde research, covering the whole spectrum of nephrology, and I have really enjoyed it. We have learned some things today about new antigens, new approaches, new mechanisms that you are going to see cited again and again and again in the literature. So, I have really enjoyed it. Not just because I had a really cool party but because it has been great to have all these people here and the nostalgia of getting together again with Ed, Bill and my other colleagues. So thank you.

Now, when Mark asked me to give this talk, I said: 'Do you want me to talk about the work in the lab? Because we have been working on intramolecular and intermolecular epitope spreading, some recent work on T-regulatory cells, and on identification of therapeutic complementary peptides in our model.' He said, 'Don't talk about any of that stuff: what I would like you to talk about is something that doesn't require very many slides, but that does give more of a perspective of where you were and how you got to where you are.' I am not used to this sort of talk. I am used to having slides that I can talk from. So, I wrote it out because that is the only way I can put all this together in an organized fashion. I apologize in advance for doing it this way, but I spent about 40 years talking from slides and not off-the-cuff without slides.

However, I have given it a considerable amount of thought. Since the turning point of my current activities from being the division chief to becoming a faculty member is a bit of a transition, it seems it is an end of one season and the beginning of another. So I entitled my talk

'Seasons'. And as I began to think more about it, there are a number of seasons. The definition of seasons that comes to mind is the four seasons, or when we think about a season, such as a time of an event, like the season of Ronald Reagan or the season of Bill Clinton. The dictionary defines season as 'a time that is characterized by a particular circumstance or a feature'. So for the last 20 years, I guess this would be the Bolton season in terms of direction of the Division of Nephrology. Add an '-ed' to 'season', and it also means that someone has become wise, or experienced, or knowledgeable by experience: 'seasoned'. Some would question whether that would fit me. But I won't elaborate.

As I reflect on my own life, there have been many seasons, some more distinct than others. Certainly my first season was my childhood and youth, which seemed to be marked by a remarkable number of spankings, standing in the corner, always being in trouble whether I was at home or at school. I climbed up a ladder when I was 4 years old and got on the roof and they had to bring in the firemen to get me down. I got in big trouble for wading in the local stream, which was also the drainage area for the sewer in our small town. I set a lot of fires that I got spanked for. I broke some windows. One of the things that got me in trouble was building homemade guns, with handcrafted rifle stocks using galvanized iron pipes and black powder and handmade lead slugs. That almost did me in when one of the galvanized pipes blew past my head instead of propelling the slug at the target. I also got in trouble for creating a homemade forge using a light reflector from a headlight of a car. I attached a vacuum cleaner blower to that, filled it up with charcoal, lit it, and

this generated enough heat to melt iron, but I almost burned down the garage. I also got in trouble for driving my car too fast, from Fincastle, where I grew up, to Newcastle, which was a little town 20 miles distant over a mountain, trying to set time records with other friends from high school who tested their cars. So that is how I spent my idyllic season of my childhood with few cares about the realities of the world.

The next season for me was a little bit more somber and a bit less sober as I went through college, trying to make up for the hard studying and work that I did and lack of social activities in high school, where I was a nerd. Fortunately my study habits were still good but the party habits were honed.

In medical school and residency, which was my next season, I worked much harder, partied much less, and became more focused. Perhaps too focused. It was at that time that I decided to go into nephrology instead of rheumatology. I began to work on autoimmune disease. As I mentioned last night, Ed Lewis, whether he knows it or not, was pivotal in that decision, as was Bill, because I had planned to be a rheumatologist until I met Ed and Bill. So Ed assigned me to work on Heymann autoimmune immune-complex nephritis (AIN), and Bill to work on anti-glomerular basement membrane (GBM) disease. We each published a couple of papers in those areas during our fellowship and for reasons that were never really entirely clear, we both left Ed's lab and we switched, so Bill went to immune-complex disease and I went to anti-GBM disease.

This was the beginning of an academic career but also another season because I moved from Chicago to Charlottesville with my daughter Kris. I began building a career and a family. These were tumultuous times with a divorce and single parenthood for a few years before I met Nancy. Once I met Nancy another season began.

Together we had three more wonderful children, Ellie, Drew, and Ben. This long season has been marked with characteristics that I think helped me in my research, my grant applications and other achievements. Since childhood I have had several characteristics that some would call good, others not so good. I was persistent to a fault and some would say to the point of being stubborn. I never knew how to take no for an answer. I always tried to figure out a way to get what I wanted. I ruffled some feathers some times, but I was usually able to get about what I wanted.

I also like to build stuff. I usually overbuild. So if I screw up, it is really hard to take apart: such as an ornamental bridge, retaining walls, a woodshed, a giant sand-

Fig. 1. Experimental model of cell-mediated immunity: 'Wattle'.

box for the kids which I later converted into a pool for goldfish, all sorts of fences, and of course, the division of nephrology, which I've enjoyed greatly.

During this time, I was devoted to raising kids, going to band performances where my daughter Kris was the drum major, various track meets, baseball games, soccer games, football games, basketball games. I coached basketball for the YMCA for a few years while the twins were playing. We won both the regional and sectional championships for each of those 2 years. So that was good. I enjoyed that.

During these years the theme was balance. Balancing my career, balancing my family, balancing the division with emphasis on clinical and basic research, clinical care, teaching, and financial security. I always felt that the key to success was not just focus and hard work, but finding a niche – like chickens. During my career I focused on anti-GBM disease, as you have heard here, specifically experimental autoimmune glomerulonephritis. There were a lot of people doing work in a similar area, mostly with antibodies, as Bill said. But not in chickens. When we presented our data on cellular immunity as the sole mediator of glomerulonephritis in chickens lacking an antibody system, I showed data illustrating an intact cell-mediated immune system. Part of that consisted of delayed-type hypersensitivity testing. We would inject the antigen into the wattle, and then measure the thickness. The question always came up: 'What's a wattle?' We figured we had to have a picture to explain what a wattle is, i.e., that red thing hanging down below the beak. So I

used to show this at meetings – it saved a lot of explaining. This is a slide that was given to me by Lee Tucker, a former fellow who worked with me on the model, on the event of my 40th birthday (fig. 1).

We also had to do kidney biopsies on these chickens to get histology for our studies. Now it turns out, for any of you who have had a piece of fried chicken recently, you will notice the kidney is covered by bone. So we had to figure out a way to chip away the bone in order to do the kidney biopsy, which is a bit of a challenge. As Bill also told you, chickens don't make urine. They actually do, but it is mixed with feces so it comes out as a paste, so we had to figure out how to separate urine and feces to measure urinary protein. This was done by putting a Foley catheter in and obstructing the passage of feces into the urine so we could collect the urine that came out. So, that's how we collected urine on chickens. That was challenging. We were persistent, focused, and we had a niche. NIH liked our chickens for a while. But then they wanted us to move on to mammals, and that is where we have been ever since.

In July of this year I stepped down as division chief; thus begins another season. This was a pivotal point and a decision that was appropriate for the time. It marked 20 years as division chief, 5 years cancer-free, and age 65. It seemed like the perfect confluence. Plus, I got a good party out of this. I was also becoming a bit tired of the normal division chief stuff and was sure Mark would be a good division chief. I felt that the division would grow, perhaps not exactly like it was before but similarly with the same general concept that I espoused. Right now, we have a couple of really cool things going on in the lab with our model of glomerulonephritis, some of it so interesting that I am not going to tell you about it. I have more time to take care of my patients and to teach on the wards. I

am still teaching on the general medicine wards, where they tell me that I am the oldest attending around, and I don't know whether they are complimenting or insulting me.

I see this new season as a bit lower key. Back to the fun stuff. I am adjusting enthusiastically to not writing the letters, the recommendations, filling out the forms, going to the meetings, and all those other things I have talked about with the other division chiefs who have stepped down.

Over the past years, I have had many seasons. Many were good, many were great and enriching. I have had my share of down times as well. But I am fortunate to have had mostly good times. I feel blessed and fortunate to be here, and to have a different perspective than I did 5 years ago. I don't know how many seasons lie ahead. I hope there are quite a few, as I still have a lot of stuff I want to get done, and a lot of time I want to spend with Nancy, my family, friends, and others, doing things. Maybe I will learn to play golf. Maybe learn to actually dance instead of shuffle. Maybe play some bridge, not to mention traveling, and I would like to build another house or two as well.

In closing, I would like to thank everybody who came last night and today. The presentations were spectacular. I don't know how to compliment the presenters more. They were just tremendous and covered such a wonderful spectrum. I want to thank the friends and colleagues who have supported me through the years. I look forward to the next seasons both for myself and my family, my friends, my colleagues, and the division of nephrology. Life is good. I have every confidence in Mark Okusa, who is picking up the reins and taking things forward, and I think this is going to continue to be a great season. Thank you.