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A conversation with Dr. Peter Agre about Nobel prizes and science diplomacy[1]

Kirsten West
Interview Editor, Statistical Journal of the IAOS
E-mail: kwestiaos@gmail.com

Dr. Peter Agre wants to educate the world about malaria! He is a molecular biologist with a medical degree from Johns Hopkins School of Medicine. He has received many honors and awards in recognition of his work. He is a Nobel laureate. He received the Nobel Prize in Chemistry in 2003. He is an elected member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences, and the American Philosophical Society. But most of all, he is known for his humanitarian efforts throughout the world, and for his humility.

In the interview, we talk to Dr. Agre about his many achievements which he attributes to the values instilled in him as a child. "Doing something that is useful is really what it is all about. You have to be motivated, dedicated and work hard." He credits his mentors with inspiring him.

We discuss the place of statistics in his work. "Without statistics we would not know if our measurements are valid." Dr. Agre is a strong advocate for science diplomacy as a way to build bridges between nations and considers it his duty as a Nobel laureate to put a human face on science, to reach young scientists and collaborators all over the world. Scientists have to interact with each other to solve global issues. He would like to see scientists get more involved with government and run for public office. He wants scientists to address the misuse and politicization of science.

Interviewer: In each issue of the Journal, we publish an interview with a person of great interest to the international community. You certainly fit the bill.

Thank you. I will try my best. Sometimes, I disappoint people. Is that all he knows?

Interviewer: I have to start out by asking about your Nobel Prize in Chemistry for your discovery when working with aquaporins – membrane proteins that serve as channels in the transfer of water. What are we talking about here? Please tell us about your discovery.

I am a medical doctor. In addition to doing clinical training, I did scientific training studying red blood cells. I worked together with my dear friend and former classmate, Vann Bennett [PhD, MD.-James B. Duke Professor of Cell Biology, Biochemistry and Neurobiology]. He is a fantastically innovative, creative, diligent scientist who has made a lot of important discoveries in terms of red blood cell membranes. He developed techniques to study the principal structural

[1]The views and opinions expressed in the interview are those of the interviewee and do not necessarily reflect the policy or position of the Statistical Journal of the International Association for Official Statistics nor IOS Press.

proteins from red blood cell membranes – spectrin, which form the girders of the membrane skeletons, and he discovered a protein named ankyrin, an attachment protein.

Even though we were classmates, Vann had already achieved a faculty position and I worked as a postdoctoral fellow with him. We were working on spectrin and we discovered that deficiencies in spectrin causes congenital hemolytic anemia.[2] The red blood cells are fragile and they break, and children can become anemic, even severely anemic because of this inherited deficiency.

We worked on the structural basis of red cells membranes and hemolytic disorders. Then, as an independent faculty member I started working on the Rhesus (RH) blood group antigens which are important in terms of blood transfusions. In pregnancies, RH negative mothers (which is about 15 percent of the population) can become sensitized to their RH positive baby and produce antibodies that can lead to the destruction of the red cells in the baby. It is an important clinical topic, but it was not understood at a basic level.

My research team was studying that and by sheer serendipity we discovered a second protein of similar size which was unrelated to RH. It was an interesting protein because it was very abundant, but nobody had seen it before. It was expressed in red blood cells and in kidney tubules. Related proteins are expressed in diverse organisms: in the lenses of the eyes, in brains of insects, in roots and stems of plants. We figured out that the second protein is the channel, the entry way to and the release of water from tissues.

We refer to this red cell molecule as Aquaporin-1. This discovery explains how cellular osmosis occurs. Rapid osmosis occurs in numerous physiological processes in humans, such as secretion of spinal fluid, sweat, and tears. It humidifies our airways, it concentrates our urine. It explains how plants take water up from the ground and transfer it to their leaves.

All this resulted in a call from Stockholm informing me that I would share the Nobel Prize in Chemistry. That was 12 years ago, in 2003.

Since then we have continued to work on aquaporins, but with the focus on malaria. It is unrelated to the initial Nobel Prize, but malaria is something I always wanted to work on, helping the poorest of the poor in developing nations. That is what I am working on now.

[2]Hemolytic anemia occurs when red blood cells die sooner than the bone marrow can produce them. The scientific term for red blood cell destruction is hemolysis.

Was it [the Aquaporin-1] an important discovery? Sufficiently important for a Nobel Prize? Well, you will have to ask the Committee. They did not ask me for my opinion on that; they simply informed me and all I had to do was to be thankful.

Interviewer: Let us talk about the reactions to you becoming a Nobel laureate. Upon hearing about the Prize, I have read that your mother advised you not to let it go to your head. Does that reaction reflect on your upbringing?

Yes. You are exactly right. My father had a PhD in chemistry and he was a professor at a small college in Minnesota. He was very eager that his sons and daughters, but mostly his sons become scientists. He was very traditional. I got a lot of impetus from him to do science. He died in 1995, before my Nobel Prize.

My mother was not from a university background. She was a farm girl. She graduated from high school and then she moved to the Twin Cities to work. She met my father. He was 11 years older. She later married him. It was one of those marriages, where you wonder how it could work given they were very different people. But they loved each other and had six children.

I am the second born, and the oldest son. I am named after my grandfather, Peter.

When the Nobel phone call came in October of 2003, a very pleasant voice, in English with a Swedish accent, informed me at 5:30 in the morning, that this was a very important phone call from Stockholm for professor Peter Agre. “Are you professor Agre?” I said, “I sure am.” Then they connected me with the Royal Swedish Academy of Sciences Nobel Chemistry Committee. I had met some of these individuals before so I knew this was not a joke. This was the real thing. They informed me that I would share the Nobel Prize in Chemistry [with Roderick MacKinnon of Rockefeller University]. I was thinking crazy thoughts like, do I tell them what a miserable chemistry student I was in high school?

I decided not to say anything about being a poor chemistry student. I was an honor student, but I was not interested in chemistry.

Then they said that there would be a press conference in ten minutes and that I should get ready for the day. My wife, Mary, always so organized, used that time to call my mother back in Minnesota to tell her that Peter would share the Nobel Prize in Chemistry and her response was: “Mary, that is very nice, but tell Peter not to let it go to his head.”

I think what she really meant is that getting prizes is nice, but doing something useful is what it is all about!

The knowledge that our mothers have! I have always taken that to heart: Getting prizes is nice, but doing something that is useful is really what it is all about.

Interviewer: Do you think her insight has something to do with her roots and your Norwegian/Swedish Lutheran background?

I think it has everything to do with her roots and also the plainspoken ways of farming people. They are practical minded. "Let us not let this get out of control here. Let us go back to work and do something useful." It reflects on her humble Scandinavian farming origin.

My father was no longer alive when I received the Prize, so he was not there to celebrate, but he was a pretty exuberant individual. I am sure it would have gone to his head. My mother was thinking of him. She would have been afraid it would have gone to his head.

I have repeated this story many times to family and friends and they all say that this is what a good Norwegian or Swedish mother would say.

Interviewer: Were you really that bad of a chemistry student?

Well, it was going through my head, but I would of course never have shared my initial thought with the Nobel Committee, but I did imagine how my high school chemistry teacher would choke on his corn flakes if he were listening to the news that morning!

Actually, I may not have been his worst student or that bad of a student, but it seemed to my father that I was underperforming in high school chemistry. I was really not that interested in the subject and I probably thought I could irritate him a little! It is not something I am particularly proud of now. It is kind of crazy, how we act out when we are young – in nutty ways.

Interviewer: So parents of teenagers, take hope?

Yes, and it also reflects on the American educational system. It is so often criticized for its poor quality, but the system gives people a second chance. In many other educational systems, the decision about whether you go on to attend a university [higher education] is made in sixth grade, when you are around the age of 10.

In the American system, you are given second chances, and for me, that was very nice. I also had some weaknesses in medical school. There were classes I did not think were very interesting – like gross anatomy. But I liked working in the laboratory. My friend, Vann Bennett, who I mentioned earlier, was a very positive influence. He taught me that studying can be fun. I consider him one of my closest friends and I always look to him for inspiration.

Interviewer: It sounds like several people have had an influence on your educational experiences and has helped put you on the trajectory to become an influential scientist. I have also read that you admire Linus Pauling?

My father knew Linus Pauling. Dad was a chemistry professor. He was very ambitious. He served on the American Chemical Society Board – the primary organization for the chemical profession and responsible for chemistry education in universities, in advocating for funding, etc.

Linus Puling is probably the greatest chemist of the 20th century. He won two Nobel Prizes, unshared. Pauling was awarded the Nobel Prize in Chemistry in 1954 for the discovery of the structures of molecules and the nature of the covalent bonds. In 1962, he was awarded the Nobel Peace Prize for his peace activism.

He won the peace prize for his efforts in nuclear arms regulations. His efforts led to the limited radioactivity test ban treaty, the treaty that prevented testing of hydrogen bombs and the releasing of hydrogen into the atmosphere. He was a famous scientist.

He was also well known to the public. He would lead protests around the White House. He was an outspoken scientist.

Pauling was actually the first person to conceive of helices in biology, that proteins can be formed from structures that are alpha-helical in nature. He predicted that deoxyribonucleic acid (DNA) would be a helix. But there was a mistake in one of his calculations. He theoretically deduced that it was a triple helix. Off by one. He was corrected by Watson and Crick.

Pauling was an eccentric, visible, highly enthusiastic person. He stayed at our house when I was a youngster. Even though that was the extent of my contact with him, it was very positive. The superstar of the universe had been to my house! It was incredibly wonderful. That is the story about Linus Pauling.

Interviewer: So even if you did not quite grasp the magnitude of winning the Nobel Prize as a child, you knew it was something big?

Actually, unlike most kids, I did know what the Nobel Prize meant at an early age. My Dad talked about it. He instilled in us that Pauling's accomplishments were the greatest and winning the Nobel Prize was the greatest accomplishment of them all. Of course, I never thought I would get one. My mother said that at the end of his life, when he was very ill, my father predicted I would get the Prize.

Interviewer: And your father's prediction did come true. Let me ask you another question. I have read an interview you gave. You said that you identify more with Huckleberry Finn than with Albert Einstein?

The question was actually whether I identified with Albert Einstein and I responded that I was fascinated by Einstein, but I never identified with him. He was a complex individual. His calculations about space and time were really over my head, and I said I identified more with Huckleberry Finn – an adventurous kid without due diligence for respecting the powers that be. Huck was unafraid to go in his own direction. That was more interesting to me. The adventures on the river, the making of a raft, camping and stuff like that.

Interviewer: Was the Nobel Prize the highpoint of your career?

In terms of visibility, it was. It drew a lot of attention. I was very often sought after for lectures before the Nobel Prize, explaining how water enters and leaves cells. It is fundamental to life, but it is only one of many processes in life. The Prize made the discovery a very visible event, brought me a bit of celebrity.

It probably changed the focus here at the University [Johns Hopkins]. I think they were a little astonished that one of their scientists could be involved in something like this. We have had two scientists [from here] win the Nobel since then. Maybe it was overdue.

Honestly, as jubilant as I felt at the time, looking back, I am very pleased to have received it, but I don't identify myself any differently from before. The things I like to do, being in the wilderness with Vann, my best friend, and being with my family, that is all the same. It was not that science was not rewarding before. And certainly, there is the expectation that everything you do will be brilliant which is probably not realistic and I think sometimes people are little bit surprised. "Is that him? He won the Nobel Prize? He does not look like a Nobel Prize winner." So there is that side.

I see the prize as a celebration of science; PR or public relations for the whole field of science; the public support of our research with research grants and the understanding of the value of the work.

It [the annual Nobel Prize awards] will happen again in about five weeks [the interview with Dr. Agre took place at the end of August 2015]. During the first week in October, the National Public Radio (NPR) – a news outlet announcing the Nobel Prize – will make it known. Medicine, physics, economics, chemistry, literature and peace – from Monday through Friday, new announcements every day.

Interviewer: Quite a week.

It is pretty exciting every year.

Interviewer: Let us also talk about your current projects. Not long after you received the Nobel Prize, you were awarded a grant to extend your studies of aquaporins to malaria. You were looking to see if aquaporins could be exploited as a means of treating or preventing the disease. It sounds like you are enjoying working on your malaria projects.

I am. It is an important disease because of the human burden. More than 200 million people will come down with malaria this year.

Interviewer: More than 200 million!

More than 500,000 small children will die of malaria and many millions who survive will be left permanently scarred, with brain damage, hearing loss, blindness, epilepsy. It is an important disease. Progress has been made and is being made, but there are dangerous signs that things could get out of hand again. So I think my work is in part, maybe, in response to my mother's de-emphasis on winning the Prize: Do something useful.

I am no longer able to do "at-the-bench" research. I have been diagnosed with Parkinson's Disease. My problem is with fatigue. I have to cut back on my travels. But I still make a lot of trips and I work in Africa some parts of every year.

I am trying to raise awareness of the malaria work done by the younger scientists. I help raise funds for their work. I am really delighted to have that role and that has been wonderful.

It is an opportunity for me to have something constructive to do now, something that might continue the effort and might indeed help a lot of poor people.

Interviewer: So you are contributing in a different way now. The world will be a better place because of your efforts.

I hope.

Interviewer: You have received honorary doctorates from universities not only in Denmark (my country). . .

I thought you sounded a little Danish. It is different from Norwegian. The Danish accent is just a little different.

Interviewer: . . . but also from Japan, Norway, Greece, Mexico, Hungary, Poland and the United States. What led these universities in different parts of the world to select you for this honor? What is the common factor?

First of all, I had colleagues or persons with whom I collaborated in many of these countries. My very first honorary doctorate was before the Nobel. It was from the University of Aarhus in Denmark. My colleagues there were wonderful scientists and wonderful human beings. They thought the work was important, and my collaboration with their scientists they thought was worthy of an honorary doctorate. That was the first one. I was absolutely delighted to get that.

Since then, there have been several other honors from places where I have collaborated with their faculty such as from the Keio University in Japan.

I did not have a direct connection in all instances. Some of the universities honored me because they thought the work is important. The occasion brings attention to their institution and to their campus and to their work. When you bring a Nobel laureate to your campus to give lectures and to meet with people, you raise the awareness of science. There is the opportunity to get it in the newspaper. You can discuss what is going on at the universities. To me, it points out that the work is important. It raises awareness. It is a positive event.

There have been more [honorary degrees]. In South America, in Peru, in Mexico, and the United States. From the University of North Carolina, where I was a postdoctoral fellow originally, from the University of Maryland, Baltimore County, where I steered a lot of their minority students to special activities, and from Penn State.

I am very happy that those events occurred. The honorary degrees are celebrations of connections I had made and connections that were to be made. It raised awareness of science. I may be naive, but I think there is a bit of responsibility here that falls on a laureate. You are still to do your best work. You should be focusing on working, but at the same time, you have an opportunity to raise awareness about science that others do not have.

In my case, now, I feel that the best work in the lab has been done. I closed it down this summer. I am 66 years old and I have Parkinson's disease. My best work is long in the past. I should focus now on other things. I still like visiting and building relationships. The honorary doctorates are often part of that. When someone proposes to you an honorary doctorate, it seems to me that it is selfish to decline it because you are too busy or it is not important enough. For them, it is a huge honor, they are provided you with their highest honor, and to say, "Thank you, I am delighted," is not too much to ask. I think it is your duty.

Interviewer: It sounds like the degrees came about in various ways, but primarily because you collaborated with colleagues all over the world.

The collaboration is what made the protein famous. We collaborated with scientists in Switzerland and Japan to solve the structure, in Denmark and in Norway to solve the sites of expression. And many of the other collaborations are with young people who came to my lab. Students came from Keio University in Japan, as an example. Students came from universities all around the world.

It is a very positive aspect of science. Science is a social endeavor. I do not know if that is realized by the public. The public might think that we scientists are all calculating, quiet people who live in dark castles and do our work at midnight. An exaggeration, of course. The international network of scientists is very powerful, rewarding and interesting.

Interviewer: And that is also a very good message for statisticians, especially statisticians working in the area of official statistics. It is easy to become isolated, focusing on your own country and your own national institute. The more you collaborate, the more you learn from each other.

Interviewer: You believe in science diplomacy. You have led multiple visits of American scientists to North Korea, Cuba, Myanmar/Burma and Iran. Tell us more about North Korea.

I have been to North Korea twice and I am planning to go back in October [2015] and again in the spring [2016] on unofficial diplomacy missions, often referred to as Track II diplomacy. We are not charged by the US government or the State Department to make these trips.

When I was President of the American Association for the Advancement of Science, triple AAAS they call themselves, 2009–2010, a new program of science diplomacy had been initiated by Norman Neureiter and Vaughan Turekian. The program is a series of science visits. As a laureate you can open doors. The North Koreans were uneasy about having American scientists visit, but when they heard the delegation would be headed by a Nobel laureate they became interested.

We made the first visit in 2009 and one year later the North Korean scientists met with us in Atlanta, Georgia at the Carter Center and subsequently at the Rockefeller [Foundation Bellagio] Center in Italy.

The events were simply scientific engagements. In 2009, they were organized by the State Academy of Sciences of the DPRK, the Democratic People's Republic of Korea. We requested the opportunity to visit 15 institutes, universities and hospitals and a few special sites, like the Great Reading Room in the Grand People's Study House. We were given permission for all of those. We met scientists, university presidents, institute leaders, and in many cases, we were the first Americans they had ever met. There is so little contact between our countries.

When I returned in late 2011, it was for a special symposium at an English language university in North

Korea, the Pyongyang University of Science and Technology. The acronym is PUST. This is a campus built because of a gift from a wealthy Korean-born business man living in Florida. His name is Kim [Kim Chin Kyung]. The event provided a mechanism for young North Korean scientists to meet American scientists.

Our visits to North Korea have been with scientists, university presidents and many young North Korean students. I must say, despite the formidable and formal way in which we interacted, we got to be friends. There are good people there. By and large, North Korean scientists have the same values and goals as American and Western scientists. They are good at science. They want to make the world a better place for their children and their grandchildren.

The scientists that we interacted with in North Korea, were all life scientists working on biological problems, nothing to do with biochemical weapons or anything that would be dangerous. It was geared towards peace related science: developing more robust drought resistant crops, new medicines, things like that.

There was negligible risk to us and lots to be gained. We have some personal contacts now and it may very well be that someday, if the political system changes, our contacts will be able to move ahead officially. We had nothing to lose by meeting them.

Interviwer: You will be in North Korea in October 2015. Are you going to lecture?

I am going to give a talk. It will all be about science. We will not get into regime change and government policy. That would not be welcomed. I want to establish friendships. I want to get working relationships. It all helps to get things to move ahead. Maintaining some kind of contact, in my view, is better than no contact.

Interviewer: It does seem so. You have to take baby-steps sometimes.

And you have to have patience.

Interviewer: Let us talk statistics. Do you use statistics in your work?

My work does not involve complex statistics. But the principles of making measurements are used. We need to establish whether the measurements are valid or not, and that is basically what statistics are about. How reliable are these observations? It has been said that "if you cannot measure it, you cannot manage it." Michael Bloomberg,[3] among others, said that speaking about business and other activities. If you cannot measure it, you cannot manage it. And in science, everything is about observations that are measured, be it weight, mass, cycle, biosynthesis of molecules. We actually are not looking for simply a yes or a no answer. It is a matter of how much? How fast? What is the structure? It is an application of the statistical method.

I think of statistics as a discipline that is trying to establish the validity of measurement. It is incredibly important to our work.

We use statistics all the time in making decisions. We can look at two data sets and see if they are different. What is the level of statistical significance of the difference? If it is not significant or only moderately so, then you know that it might not be a true difference. If the statistical significance is quite clear, 1 chance in 1,000, then we are all set. If what you are observing is not a co-incidence then you can feel confident about moving on. The statistical test is a fairly practical assessment of reality. We need that. Very much so.

I am also a big fan of biostatisticians! We have a department here at the Bloomberg School of Public Health that are producing trends from the data. Something that is widely viewed are the Kaplan-Meier plots. The Kaplan-Meier estimator is known as the product limit estimator. It is a non-parametric statistics used to estimate the survival function from lifetime data.

And in my malaria work, I use projections and estimates all the time. When I tell you, there are more than 200 million people that have malaria where do those numbers come from? We use projections. We say there are over 600,000 deaths. Again, where do these numbers come from? Nobody counted all of them. Again, we collected data from dozens and dozens of countries around the world and looked at them and came up with what is the best estimate. The range is probably from 450,000 to 800,000. That is as good as it can get.

The final control of malaria will be achieved by public health physicians and scientists. There will be a lot of statistics involved.

Interviewer: It is good to know that statisticians are appreciated.

Yes, the field is certainly not romanticized and being involved with statistics is not the most romantic type of work. You will be hard pressed to see statistician as a role for a Hollywood movie star.

Without clear validity, it is difficult to make important decisions. Take the reaction to medicines. Is it a statistically significant correlation? To prove protection or lack of protection you need to be very rigorous. That is something the statisticians can provide.

[3] Michael Bloomberg was the Mayor of New York City (2002–2013). He has donated one billion dollars to Johns Hopkins University, including funding for the Johns Hopkins Malaria Research Institute. Mr. Bloomberg has taken an interest in genetically engineering mosquitoes to prevent the transmission of malaria.

Scientists are in a sense trying to sell something, their discovery that they think is important. Statisticians are saying, "Yes, but not so fast." Prove it first.

Interviewer: I am going to change to a completely different question. I have watched a recording of your appearance on the Colbert Report. Do you remember the exchange you had with Colbert after he saw your Nobel Prize medal? He wanted to exchange all the prizes he had won over the years for your medal. You said you would make the trade, if he would let you host the show for two weeks. Who would you have brought on the show, had this been a serious exchange?

Oh, it was just a joke. My appearance was just before the election in 2008.

Interviewer: Yes, I believe this was around the time when you were involved with Maryland politics?

It was actually Minnesota politics. At the time, there was a run for a senate seat in that state. The US senate is a very important institution. I was not making a grandiose acclamation. I was concerned that my home state of Minnesota had a senator who had basically changed his tune from being a progressive liberal to a conservative Bush supporter and the Democratic party, my party, did not have a candidate. Al Franken [American comedian, actor, and writer] was going to run, and did run and in the end, he was appointed the senator from Minnesota.

Statisticians can look at that election and say there is no clear winner. After a recount and six months of legal battle Franken won by 312 votes out of 3 million votes with many disqualified ballots. We don't really know who won the election, but my interest was really in being able to advocate for education, the environment and most of all for health care. Al Franken was elected because he said that he did not like George Bush and he was against the war in Iraq – not much of a platform, but it was enough because of the Obama landslide in Minnesota.

But back to the Colbert Report. They had me on the show because I was a founding member of Scientists and Engineers for America (SEA). We were to talk about sound science in politics, the decline of American knowledge of science, among other topics. I got so much positive feedback from the Colbert Report appearance. I got so much encouragement. It made me want to run for political office.

There will be occasions where people with a science background will choose to run for public office. I think that can be a very good thing. I explored it, but I never formally ran for office. I was hesitant because as a university faculty member to run for office, I would need to take a leave of absence, and I am not a wealthy person. I don't have private wealth to pay for health care. That would have been the very first step. I was cautious. As soon as I contacted people in Minnesota, a lot of interest emerged particularly from senior statesmen such as Walter Mondale, and Wesley Clark, and Tom Daschle. None of them told me not to do it. I explored it, and in the end, I decided to stay where I was, doing what I loved and still love – science.

The politicians come and go and the problems are usually still there after they have left office. If we have some good people with technical and scientific training in office that could perhaps help. I hope young scientists will consider running for political office at some point perhaps later in their careers. Just a few of them. It would help a great deal.

Interviewer: What are some of the important lessons you have learned from engaging with politicians and political leaders in different countries all over the world?

I try very hard to communicate a sense of gratitude for the support given to scientists. Politicians are looking out for their constituency and are eager to be reelected. And sometimes the reelection process takes precedence over everything else. But I always try to thank them for their support of science and remind them of the value of their continuing investment in science and the need for top quality science. The issues facing them and us often times have scientific answers. Take malaria!

Interviewer: How do official statisticians manage in the real world where the budgets are controlled by the politicians? What advice would you give them?

Being morally correct is important, but being convincing is essential. Make the pleas for a program, but make it convincingly. The official statisticians need to convince the politicians that it is in their best interest to fund them.

Interviewer: If you were the key note speaker at the annual meeting of the International Association for Official Statistics what would be the title of your talk? What message would you like the audience to take away from the speech?

I would want to talk about science opening doors worldwide. I speak about this a lot. I see statisticians as scientists, an engineering form of science. You evaluate something and you access the reliability. That is clearly science. Biostatistics and other forms of statistics are important in all countries. Opening doors, whether you are a molecular biologist or a statistician, is the same opportunity. Use the opportunities you are given to do that. That is what I would lecture about. That would be my message.