

From International Leadership in Cardiac Disease to a Focus on Heart Health

A Conversation Between Valentín Fuster and Marcelo Di Carli

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Marcelo DiCarli, MD, a Professor of Radiology and Medicine at Harvard Medical School/Brigham and Women's Hospital (Boston, MA), interviewed Valentín Fuster, MD, PhD, about his long career as an international leader in cardiology. Dr. Fuster obtained his MD from the University of Barcelona (Spain) and PhD degree from the University of Edinburgh (Scotland) awarded in Barcelona (Spain). He was Professor in Medicine and Cardiovascular Diseases at the Mayo Medical School (Rochester, MN) and later at the Medical School of Mount Sinai Hospital (New York, NY). He was the Mallinckrodt Professor of Medicine at Harvard Medical School and Chief of Cardiology at the Massachusetts General Hospital (Boston). In 1994, he was named director of the Cardiovascular Institute at Mount Sinai, a post he has combined since 2012 with that of Physician-in-Chief of the hospital.

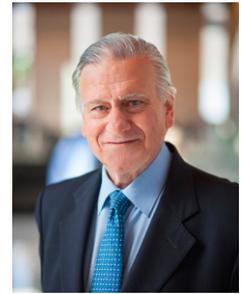
He has served as president of the American Heart Association (AHA) and the World Heart Federation; is a member of the U.S. National Academy of Medicine, where he cochaired the Advisory Committee on the Role of the United States in Global Health; was a member of the European Horizon 2020 Scientific Panel of Health; was a council member of the National Heart, Lung, and Blood Institute; and was president of the Training Program of the American College of Cardiology (ACC). He has published more than 1,000 scientific articles over more than 50 years and currently serves as editor-in-chief of the *Journal of the American College of Cardiology*. He has received many awards, including the Prince of Asturias Award for Technical and Scientific Research, the Grand Prix Scientifique of the Institute of France, Gold Medal and Research Achievement Award from the AHA, the Living Legend and Life Achievement Award from the ACC, the Gold Medal from the European Society of Cardiology, and the title of Marquis from King Juan Carlos I of Spain. In addition to his dedication to research, Dr. Fuster is strongly committed to communicating to the public, which led to the launch of the Science, Health, and Education Foundation, of which Dr. Fuster is president, directed at improving public health, especially in the young. *The Resilient Heart*, a documentary about his international work with children, premiered at the 2017 Tribeca Film Festival in New York.

Dr. Di Carli: Although you grew up in a family of physicians, my understanding is that medicine was not your primary interest. How did you discover that medicine was going to be your future?

Dr. Fuster: I had a passion for tennis and played at the national level in Spain. There was a possibility to go to the Orange Bowl in Miami—the young Davis Cup. The manager of the team told me that I needed to win a tournament to make the team. I lost the tournament and the possibility of joining the team. I suddenly realized that it was going to be difficult to make it in tennis. I was lost, except that something I really liked was researching plants and the environment, so I wanted to study agriculture. However, the problem at that time was that it was uncommon to move too far from your city and your family, and there was no school of agriculture in Barcelona. It was at the tennis club in Barcelona that I met the Spanish physician with the highest reputation at the time, Pedro Ferreras Valentí, MD, who was an author of the classic Spanish textbook of internal medicine. It was Dr. Ferreras who told me that I should be a doctor. I had no idea what he was talking about or why he would say that. But, you know, I learned in life to trust certain people, and, not knowing what to do with my life, I followed his advice. Dr. Ferreras became my instant mentor. He had a heart attack at age 45, and at the time he encouraged me to become a cardiologist, which he felt was the only subject in medicine he didn't know well. This story goes on . . . I am a complete product of mentorship, which involves trusting someone who really cares about you and who drives you. I think my life became easier because I just listened to these people. That's basically how I went into medicine.

Dr. Di Carli: Fascinating story. How did you get into cardiology and acute myocardial infarction research?

Dr. Fuster: This is very interesting. Basically, my mentor told me that every summer I should go out of the country and learn basic science, which, at that time, was simply histochemistry. I went to Liverpool (U.K.) to study with a well-known pathologist, Harold Sheehan, MD, DSc. I arrived there as a student, and he asked me to join him every afternoon to look at pathology slides. The first day he showed me a pathology slide that was basically a blood clot full of platelets obtained from the coronary artery of a patient who had died



Valentín Fuster, MD, PhD

of a heart attack. I asked him what a blood clot and platelets had to do with a heart attack. He responded, “We don’t know if clots are the cause or the consequence of a heart attack.” This was around 1963. He suggested that I investigate this question for my thesis. Why did he suggest this? Don’t ask me. But it is exactly what I did. I went to the University of Edinburgh to do my PhD and investigated the function of platelets to understand how heart attacks occur. This is yet another example of how I got into this field: by talking to the right person about a single pathology slide.

Dr. Di Carli: This concept of strong mentorship resonates very loudly with these 2 stories—first medicine and then cardiology and heart attacks.

Dr. Fuster: Can I tell you how I got into imaging?

Dr. Di Carli: How was that?

Dr. Fuster: After Edinburgh, I went to the Mayo Clinic, where I began to look at blood clots in the arterial lumen and reached the conclusion that I needed to study the relationship between blood clotting and the vessel wall. It turned out that my brother, a neuroscientist at the University of California at Los Angeles, was working with MRI of the brain in monkeys. I was very impressed with this imaging tool and wondered whether instead of looking at the brain we could just focus on the arteries. I went to the Massachusetts General Hospital and used postmortem MRI to look at the vessel wall. That’s how I got interested in imaging, which started by examining the vessel wall at autopsy.

Dr. Di Carli: Is being a good listener and having a good mentor all you need to have a successful research career, or is there more to it?

the one contribution of which you’re the most proud or that that you cherish the most?

Dr. Fuster: Let me rephrase your question. If someone asked me what my most important life contribution has been, I have no doubt that the answer would be “mentoring young people.” The VF Society, comprised of more than 200 people that I have mentored, is now more than 2 decades old. We meet every other year, and, to me, that is by far the most satisfactory aspect of my professional and research career. Recognitions and awards are great, but they are short-lived. Instead, what you do for mentees is for life. I’m obsessed about that. Why? Because I was mentored as a young person, and I am a product of what you and I are talking about. That is to me the most meaningful aspect of my career that I feel most happy about.

Dr. Di Carli: We’re completely in agreement. If you were to start your career over, would you do anything different?

Dr. Fuster: When I decided to study medicine, my father was a psychiatrist and my brother a neuroscientist. They both said that I should focus on the brain. I disagreed, because I did not think there was anything tangible in the field at that time. I told them that I did not share their excitement. Today, I would respond differently. In fact, half of what I do today is focused on the brain. If I had to start over again, I would focus on neuroscience, because we are on the verge of great discoveries related to the brain, which 50 years ago few people really anticipated.

Dr. Di Carli: Let me switch gears a little and get into your extraordinary accomplishments in imaging. I don’t know many clinical scientists who have done so much imaging without being

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Dr. Fuster: You need to have curiosity. This is something that you’re born with—either you have it or you don’t. Not everyone can be an investigator. You also need the environment and the mentorship, and these 2 are closely interconnected. Basically, you need to be in a culture that stimulates your curiosity. The next thing is to pass what I call the stress test. As you begin a research career, there are many frustrations, including experiments that don’t work, papers not accepted, grants not funded, and other obstacles. This is a crucial test that helps define who will be an investigator and who will not. If you can go through this stress test and persist with resilience, you will likely be all right.

Dr. Di Carli: You raised a very important point about resilience. The frustrations you outlined above and failure of the stress test can very easily discourage someone from pursuing a research career. Is there anything else you would advise?

Dr. Fuster: I left tennis in a single hour, because I had the intuition that I was not born for it. But if you’re really born with the curiosity for research and have the right guidance, with a positive intuition you can go through these stress tests and overcome the frustrations and setbacks. That means that you are there and born for that. These setbacks help you mature, and this is very positive, because it signals that you are on the right track.

Dr. Di Carli: That’s a very important message for our young audience. You are an amazing clinician/scientist and among the most successful people in the world in clinical research. What is

an imager. What do you predict will be the ultimate role of imaging, both in clinical practice and in research?

Dr. Fuster: I believe that 5 fields will drive discoveries and treatment in the next 20 years. Number 1 is imaging, because it allows us to see at the molecular and anatomic levels. I have been working with risk factors associated with the number 1 killer for many years and observing risk scores. Unlike risk factors, however, imaging gives us a direct window into the disease and tells us what is actually there, even in the early stages. Genetics will also be very important but will take some time. Artificial intelligence will drive discoveries and assist in patient care. Then there is the study of a single cell; for example, the circulating macrophage, providing information on genetics and so forth. Finally, enhancement of defense mechanisms via new developments in the field of pharmacology will be very important. But, without question, imaging will be number 1 because it tells us what is there in a tangible way. Likewise, molecular imaging will provide an opportunity to understand disease mechanisms and help assess response to therapy.

Dr. Di Carli: Getting into atherosclerosis, you coined the term “vulnerable plaque,” which has been the focus of intense research for the last 20 years. Do you think this paradigm is still relevant?

Dr. Fuster: It is less relevant, but let me explain. The concept of vulnerable plaque was developed after we became involved with post-mortem MRI. It was useful to understand the different stages of the atherosclerotic plaque within the arterial wall. Later, the introduction

of intravascular imaging gave us a more detailed understanding of the natural history of atherosclerotic plaques. I would say that the concept of vulnerable plaque was useful to understand the pathophysiology of atherosclerosis and its complications. However, now we know that there are too many vulnerable plaques. So, our clinical focus has shifted to the burden of disease, which has much more power in predicting who is at higher risk for adverse events. Imaging through the combination of PET and MRI continues to provide pathophysiologic insights. We have studied more than 900 people with PET/MRI and are learning more about the role of inflammation in vivo in the initiation and progression of atherosclerosis.

Dr. Di Carli: What do you think is the future of cardiovascular molecular imaging? Will it be a research tool, or do you think that it may find a translational niche to help identify people at risk?

Dr. Fuster: Molecular imaging started as a powerful research tool, but this is rapidly changing. For example, at a clinical level molecular imaging now plays a key role in sarcoidosis, infective endocarditis, and amyloidosis. I predict that in the future, when we need to know if there is a clot somewhere in the body, there is no question that molecular imaging is going to give us the answer. There is intense focus on the role of inflammation assessed by PET in the arteries, including the coronary arteries. We are also using PET to learn about what is going on in the brains of patients with risk factors and decreased flow. In my opinion, molecular imaging will continue to expand as a critical imaging tool in patient care.

Dr. Di Carli: It's been very impressive to see your efforts in community education and engagement for prevention of cardiovascular disease, including community-based randomized clinical trials. What motivated you to get into this line of research?

Dr. Fuster: About 10 years ago, after having worked for so long on clinical disease and belonging to organizations that talk constantly about preventing disease, I became somewhat skeptical about the adequacy of our efforts to prevent cardiovascular disease. I felt that there was a lot of talk but very little action or results. I realized that we knew more about disease than health. I personally started with a clot, then I went into the vessel wall with imaging, and then I realized that what's in the vessel wall results from human behavior. So, I transitioned from the very end to the very beginning of the disease. The question was where disease begins. Imaging again was very important in this transition. We started using 3D vascular ultrasound to study the whole arterial system externally and learned that we can identify subclinical disease in healthy people at a very young age, at 20–30 years old. In our bioimaging study, the burden of subclinical disease detected in healthy individuals was related to events 12 years later. Similarly, in the Coronary Artery Risk Development in Young Adults (CARDIA) study, a longitudinal epidemiological study that follows healthy people into their 80s, we showed that

poor control of cholesterol between ages 20 and 40 was linked to events as young adults. This suggests to me that what we consider healthy or normal is already very abnormal at younger ages with the accumulation of risk factors and subclinical disease. This is important, because most of our prevention guidelines start emphasizing control of risk factors at age 40. It is clear to me that this is already too late. So, we launched several clinical trials in younger people with subclinical disease, starting at age 20. And then we got into randomization of towns to test the efficacy of various interventions, including education, exercise, and stress management. Now we are working with 50,000 children, all randomized at different ages with different educational strategies, because I am convinced that this is the time when people listen. Later in life, we don't listen. As you can see, I am excited to devote my effort to the field of health, not only because we are learning a great deal about the beginning of disease but also because I am convinced that this is where we should focus our preventive efforts. We are also gaining a new appreciation of all the defense mechanisms that we have ignored for so long. I believe that this is really where the future of pharmacology will be.

Dr. Di Carli: This is truly fascinating. Before I let you go, what are your goals for the next decade?

Dr. Fuster: As I tell young people, I want to continue to be creative and to see where I can help. I am vested in and very committed to all these projects that I mentioned, because I believe we can do something meaningful in global health and trigger change. The second thing is that, like all of us, I want to be happy. By that I mean that I continue to invest whatever talents I have in helping others. That to me is critical and makes me happy. The third goal is to continue to invest in team effort. I believe very strongly in horizontal systems. In fact, I don't care what position I have, because I believe that the person who cleans the floor in the morning is like me but just with a different job. In this team effort, I try to enhance the role of young people, who are as important as the senior members in the team. I realize that life is not easy. We are all going through a very difficult time. But within that context, we try to do the best we can. My message to a young audience is invest in what you are passionate about and interested in and listen to your mentors.

Dr. Di Carli: This has been a most inspiring conversation. It is clear to me that one of the reasons you have been so successful is that you are genuine and capable of explaining things in simple words that people of all ages and backgrounds can understand and relate to. Every time I speak with you, you remind me of one of my own mentors, René Favaloro, MD, because of your simple and genuine talk and big ideas. I suspect that this is why the VF Society has so many members—because young people can really relate to you not only in the medicine that you practice but also in the life you live. Thank you very much.