

A conversation with Eugene Braunwald

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Conversations with Giants in Medicine

Eugene Braunwald (Figure 1) is often called the father of modern cardiology, as he was the first to define the pathophysiology of hypertrophic cardiomyopathy and to demonstrate the salvage of ischemic myocardium following coronary occlusion. The full interview, with many more stories about performing in the opera and his seminal research discoveries, can be seen on the JCI website, <http://www.jci.org/kiosk/cgm>. JCI: Can you tell us about your path to medical school? Braunwald: I was born in Vienna, Austria, and had an idyllic childhood there with an excellent school, and tutors in English and piano. On March 12, 1938, everything changed because Austria was annexed by Germany. The Nazis came in, and the fury against the Jews played out in a matter of days. It was a very troubling period. We escaped from Austria at the end of July 1938 with a couple of close calls. It was like *The Sound of Music* — except that there was no music. We ended up in London two days later, literally with just the shirts on our back. When war was declared in September 1939, my brother and I were evacuated to a small village in Northern England. After living with a wonderful family for a couple of months, I got a postcard that our family was going to America. We took the [...]

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JCI: Can you tell us about your path to medical school?

Braunwald: I was born in Vienna, Austria, and had an idyllic childhood there with an excellent school, and tutors in English and piano. On March 12, 1938, everything changed because Austria was annexed by Germany. The Nazis came in, and the fury against the Jews played out in a matter of days. It was a very troubling period. We escaped from Austria at the end of July 1938 with a couple of close calls. It was like *The Sound of Music* – except that there was no music. We ended up in London two days later, literally with just the shirts on our back. When war was declared in September 1939, my brother and I were evacuated to a small village in Northern England. After living with a wonderful family for a couple of months, I got a postcard that our family was going to America. We took the President Harding, which was one of the last passenger ships to cross the Atlantic because the German U-boats were out in force.

We landed in New York and, after completing grammar school, I landed at Brooklyn Technical High School. I wanted to be an engineer, a field that reigned supreme during WWII. But, then I thought it was too impersonal and chose medicine. Engineering concepts came in handy when, in medical school, I developed an interest in cardiology because cardiologists were either “electricians” or “plumbers” – i.e., used concepts from electrical or mechanical engineering.

JCI: You took an elective in your last year of medical school that introduced you to cardiology.

Braunwald: When I entered my senior year at NYU Medical School in 1951, research electives were not a standard part of medical education in the US. However, I was able to take an elective with Ludwig Eichna, who directed a cardiac catheterization laboratory at Bellevue Hospital. Cardiac catheterization is now a diagnostic technique that’s

carried out in probably 4,000 hospitals in the US. But, at that time there were only 12 cardiac cath labs in the country. It was an eye-opening experience, to be in a serious research laboratory, and I became interested in the pathophysiology of heart failure.

Later, I had a postdoctoral fellowship with [Nobel Laureate] André Courmand, who also worked in Bellevue Hospital, but in the Columbia University division. I spent a year there and that firmed my interest in research, and also led to my being accepted by what was then the National Heart Institute. That discharged my military obligation, as there was a doctor draft during, and after, the Korean War.

The NIH years, which were from 1955 to 1968, provided such a rich environment in terms of ideas, and the fact that there were incredible colleagues and tremendous opportunities for interaction with outstanding scientists in all areas of biomedical science. My assignment for the first two years was in the Laboratory of Cardiovascular Physiology with Stanley Sarnoff, who was a brilliant physiologist who introduced me to a whole new way of thinking about the circulation. We began to determine how much energy the heart needs to do its work. We learned a lot over the course of 13 years about oxygen consumption and ischemia – how ischemia causes angina and how ischemia can cause a full-blown myocardial infarction.

JCI: What lead you to your major discoveries?

Braunwald: I’ve had basically two “aha” moments which came close together, the first in 1967 and the other in 1968. In 1967, I met Seymour Schwartz, a surgeon at the University of Rochester, and he showed me a colony of dogs in which he had produced experimental hypertension. He had implanted an electrical stimulator on the carotid sinus nerves, and this was effective in reducing the elevated blood pressure. Carotid sinus stimulation also slows the heart rate and reduces myocardial contractility. What occurred to me, on my way home from Rochester, was that carotid sinus nerve stimulation might be an effective way of reducing myocardial oxygen consumption, and might therefore be a great way of treating intractable angina. From the conception of the idea to the first patient treated took six weeks. Patients would turn the carotid sinus nerve stimulator on and this would

give them relief from severe angina. We were in discussion with developing a large phase 3 trial to get this device approved for marketing, but coronary artery bypass graft surgery came on the scene and was superior to carotid sinus nerve stimulation in relieving angina. But, all was not lost because it led to my second, and more important, “aha” moment in the spring of 1968. We told our patients that if they had unusually severe pain, not the usual angina, they shouldn’t turn their carotid sinus stimulators on because, if they were having an infarction, we didn’t want their blood pressure to drop. One of our patients, who had a stimulator, came into the Clinical Center with severe chest pain and the ECG findings of an ongoing myocardial infarction. He did not listen to my advice and he kept the stimulator on.

That evening, when I looked at the ECGs recorded while he had his myocardial infarction, I found that it varied in an interesting way. When the stimulator was turned on, the ST segments – the part of the ECG that reflects ischemia – were almost normal. When I came along and turned the stimulator off, it became more abnormal. This happened several times over the course of two hours. So, he was right and I was wrong. This meant that even several hours into a myocardial infarction you could still manipulate the severity of ischemia. The traditional thinking had been that myocardial infarction was a sudden event. It was thought that a clot in the coronary artery that killed heart muscle was like turning a light switch off. What the experience with this patient suggested was that maybe myocardial infarction was more like turning light down with a dimmer, and that you could save heart muscle in the course of a heart attack. Our subsequent dog studies found that it was possible to do that, and we began to publish on techniques for protection of the ischemic myocardium and the reduction of infarct size. Those dog experiments showing that infarct size could be reduced really put me on a different path, and this led to our attempts to apply the same principles to patients, which has been a major subject of my subsequent research.

JCI: How did you come upon the discovery and description of hypertrophic cardiomyopathy?

Braunwald: That was an extraordinary experience. In 1958, we studied a young man at the NIH who had a loud heart murmur



Figure 1
Ushma Neill interviews Eugene Braunwald on October 23, 2012, in New York City. Image credit: Semyon Maltsev.

and shortness of breath with a large pressure gradient between the body of his left ventricle and the aortic valve. We assumed that he had a congenital subaortic stenosis, a pretty uncommon congenital condition, and that he required open heart surgery. On the morning of his operation, while I was doing a cardiac catheterization, a message came down from the operating room that my surgical colleague, Glenn Morrow, wanted to see me in the OR immediately. It was a little awkward because I had a patient on the table. I came into the operating room and Morrow was bent over the patient, and he said, “You know, Gene, you’ve screwed up. He doesn’t have a subaortic stenosis. I arrested his heart,” which was a big deal at the time and quite risky. He opened the aorta, and put his index finger through the aortic leaflets, down into the body of the left ventricle. With his left hand, he put his fingers through the left atrial appendage through the left atrial cavity, and into the left ventricle, and his two index fingers met in the left ventricle. There was no obstruction!

I was shocked and confused and blurted, “I don’t know what happened but I have a patient on the cath table.” And, as I walked out of the OR, I said, “But Glenn, if you get his heart started again, please stick a needle into the left ventricle to see if he still has a pressure gradient.” Morrow came down a couple of hours later to say that when he restarted the heart he confirmed a large

pressure gradient. We puzzled about that, day in and day out, for a couple of months, when a second patient presented with identical findings. We didn’t know exactly what was going on, but in our initial paper we suggested that the subaortic obstruction was caused by left ventricular hypertrophy. These two patients led to our intense interest and further study of this condition.

We used all of the tremendous opportunities at the NIH to study these, and many other, patients by the best imaging techniques that were then available, though pretty crude by today’s standards. We reported that the condition was frequently familial, associated with sudden death, and most interestingly, we found that the obstruction was dynamic. Any influence that reduced the size of the ventricle, such as β -adrenergic agonists, intensified the obstruction. And, any intervention that increased the size of the ventricle, such as raising the blood pressure, reduced the obstruction. Beta blockers were just developed, and we were able to show that they reduced obstruction and improved exercise tolerance. Now, about 55 years later, beta blockers remain a mainstay of therapy.

JCI: You’ve described your 13 years at NIH as a virtual Camelot. So, what motivated you to take a job at UCSD helping to found their department of medicine and serve as its first chair?

Braunwald: I became a little restless. And it’s like saying, “Well, I like steak. But,

I don’t like steak three meals a day, seven days a week.” And, I began to feel a little bit about research that way. I became interested in medical curriculum development, and what better way is there to do that than at a new medical school?

JCI: You then moved on to be Chairman of Medicine within the Harvard system for 24 years.

Braunwald: I had four very good years in La Jolla. But the problem was that the new governor of California, Ronald Reagan, made a decision not to build the school’s university hospital. I felt that we could not develop a great medical school without a great hospital. So, when the opportunity in Boston came along, I took that. My period in California prepared me for a much tougher job, and that was at the Brigham, which required a lot of reorganization and an emphasis on graduate medical education.

JCI: In addition to the over 1,000 research articles you’ve written, you served as editor of Harrison’s Principles of Internal Medicine for twelve editions and you’re now on to the ninth edition of Braunwald’s Heart Disease, the definitive textbook of cardiology.

Braunwald: I think that textbooks are important in terms of education. One of the things that gives me the most satisfaction is when I get a letter from a physician in India or Pakistan saying, “Dear Professor, your book is very important to me and we use it constantly but I’d like to point out to you that on page 1372, in the second paragraph in the left column, you say that this drug causes hypotension. With all due respect, sir, it causes hypertension.” And so, what does that mean? It means that the book provides the capacity to reach out to many more people than you can reach when you stand before a class. By the way, those letters, of which I have received hundreds over the years, are usually correct, and the text is corrected with thanks to the letter writer.

JCI: Have you ever given a thought to a different career, or was it always medicine and always cardiology?

Braunwald: Yes, it has because I’ve always really been challenged by the wide variety of things that I’ve been able to do. In addition to research, teaching, and textbook editing, I have also enjoyed the practice of cardiology. I’ve been constantly stimulated, and I am as excited today about issues surrounding myocardial ischemia and heart failure as I was when I was introduced to them as a medical student more than 60 years ago!

Ushma S. Neill