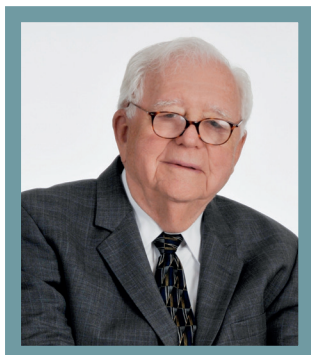


Featuring: Eugene Braunwald



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In the Cardiology Masters section of *European Cardiology Review*, we bring you an insight into the career of a key contributor to the field of cardiology.

In this issue, we feature **Professor Eugene Braunwald**, cardiovascular medicine specialist at Brigham and Women's Hospital and distinguished Hersey Professor of Medicine at Harvard University, Boston, Massachusetts, US.

Eugene Braunwald is a cardiovascular specialist at Brigham and Women's Hospital. He studied cardiology at the New York University School of Medicine before completing an internal medicine residency at the Johns Hopkins Hospital and a cardiology residency at Mount Sinai Hospital. He went on to complete cardiology fellowships at Columbia University College of Physicians and Surgeons and the National Heart Institute.

As the founding chairman of the Thrombolysis in Myocardial Infarction (TIMI) Study Group, Prof Braunwald and his colleagues have provided significant insight into the treatment of patients suffering from acute MI and unstable angina.

Prof Braunwald has been listed as the most frequently cited author in cardiology by Science Watch. He has served as an editor of *Harrison's Principles of Internal Medicine* for 12 editions and is the founding editor of *Braunwald's Heart Disease*, now in its 11th edition, as well as two other prominent cardiovascular textbooks.

I was eight and a half years old when the lights of my childhood went out. It was 1938 and my family and I lived in what had been, until then, a pleasant area in the first District of Vienna near the Danube Canal. I went to a special school, took piano and English lessons and had good friends. My mother often took my younger brother and me on walks around the canal. We watched the boats and other activities on the water and had picnics in the park. My father ran a successful wholesale clothing business and he and my mother were devoted opera fans. They began taking me to Vienna State Opera when I was 6 years old, sparking a love of music that I carry with me to this day.

It was a wonderful life. I was too young to understand what was happening just across the border in Germany.

Sudden Darkness

My memories of how that period ended – on 12 March 1938, with the Anschluss, of Austria – are vivid. The Nazis marched in and, insofar as the Jews were concerned, accomplished in 5 days what had taken 5 years in Germany. The park benches we had sat on were – overnight it seemed – painted with large yellow letters that said, "Jews must not sit here". I saw elderly Jews, with armed policemen standing over them, being forced to clean the pavements in front of their homes with their toothbrushes. Aware of the growing danger, my parents took me out of school.

My younger brother Jack and I were largely confined to our home, frustrated and bewildered by this dark change in our lives.

A couple of months later, the Nazis came for my father in the middle of the night and my mother woke us up to say goodbye to him. "He's going away," she wept. My father, deathly pale, could barely speak. He packed up some belongings and hugged us for what he imagined could be the last time. However, it was not – thanks to my brilliant and quick-thinking mother.

The next day, the SS officer who had been liquidating my father's business (and taking the proceeds) arrived and asked, "Where is the Jew?" My mother, still weeping, explained that he had been taken away, but added, "You still need him! You've only liquidated half of the business." It was true. The SS officer got on the phone and a series of arguments ensued. It seemed the train carrying my father had not left the station. He was brought back to our home. He had been away for less than 10 hours. It was miraculous. However, my parents knew it was only a matter of time before he would be sent to a concentration camp. We had to get out.

Anxious Escape

On a Saturday morning in late July 1938, my mother came into our bedroom and said: "Boys, you have to get dressed quickly. We're

going on a picnic.” That struck me as odd, but when I began to ask questions, she cut me off quickly. “Just do it,” she said. She had a basket of food and the four of us boarded a trolley, then a taxi that took us to the train station. From there we took a train to the Swiss border and, as I recall, were met by a man who – for a significant price, I would guess – saw to it that we got across. It was terribly frightening. At that age, you want to believe your parents are in control, but it was clear to me that they were afraid and certainly not in control of our lives. From Switzerland, we took a train to Paris, then another to Calais. Finally, we ferried across the English Channel and reached London. The whole ordeal lasted about 48 hours.

A Year of Stability

We arrived in London with the clothes we had on and virtually nothing else. We were met there by representatives of the Jewish Relief Agency, who set us up in a two-room apartment in a low-rent part of the city. Within days, my parents had jobs wrapping packages in the basement of Selfridges department store. I had learned English from my tutor in Vienna, so I was the only one in the family who spoke the language. This meant I was entrusted to negotiate the buying of milk and bread in the grocery shop. However, my parents immediately began taking English lessons and caught up quickly.

Our family life was relatively stable again for about a year. Then, in September 1939, World War II began. My brother and I were among the hundreds of thousands of children who were evacuated from London. We were each given a basket with a gas mask and a chocolate bar and then removed to the comparative safety of the English countryside.

Jack and I were housed with a family of farmers, the Whites, in a village near Northampton. The accommodation was modest – there was no indoor plumbing – but the family welcomed us and treated us kindly.

We were refugees and the UK saved our lives. However, a bureaucratic quirk soon forced us to move again. After a few months, I received a telegram from my father with explicit instructions. I was to buy third-class tickets for my brother and myself and catch a train from Northampton to London, leaving on a specific day and time. My father would meet our train in London and, several days later, we would begin our journey to the US. The reason for this was that Austria had been annexed by Germany, not conquered. As such, we were technically now German citizens, and enemy aliens in the UK. My father was to be placed in an internment camp; not a concentration camp, but a camp surrounded by a barbed wire fence, nonetheless.

My parents had arranged with distant relatives of my mother in New York that they would serve as our US sponsors, guaranteeing that we would never become wards of the state. We boarded the *President Harding* passenger ship and crossed the Atlantic; a trip that would soon be far more treacherous because of the proliferation of German U-boats. Our new home was in Brooklyn.

Aspiring Engineer

Our traumas finally behind us, I finished grammar school in Brooklyn and attended Brooklyn Technical High School, an elite high school. The war was nearly over and I was planning to go into engineering, which was the most popular profession of the day. However, after a couple of years, my interest in engineering began to wane; I felt that the human

Figure 1: Dr Braunwald in the 1960s with ECG Tracing



Source: US National Library of Medicine, National Institutes of Health.

element was lacking. This realisation led me into medicine. I remained interested in pumps and electromagnets. In medicine, you cannot get any closer to engineering than cardiology.

From there, I went on to New York University (NYU), where I met my future first wife, Nina Starr, who would become a renowned cardiothoracic surgeon. Together, we went through college and then NYU School of Medicine. We married in June 1952, between graduation and internship.

Better Luck

As challenging as my childhood was, I have been extremely lucky since then. From the day I was accepted to medical school – 1 May 1948, almost exactly 10 years after that dark day in Vienna – I have somehow always managed to be in the right place at the right time, with the right people, in the right institution.

By the 1960s I was active in research and clinical work, and my family and I moved several times (*Figure 1*). We started in New York, then spent 13 years in Bethesda, Maryland, where I was the Chief of Cardiology and Clinical Director of the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH). Through Nina, I met the man who was probably my greatest mentor, her boss, Dr Andrew Glenn Morrow.

Next came 4 years at the University of California (UC), San Diego (1968–72), where I was the founding Chair of the Department of Medicine. In 1972 I went to Boston as Chair of Medicine at the Brigham and Women’s Hospital and Harvard Medical School (*Figure 2*). My family and I have lived in Weston, a Boston suburb, since then.

Figure 2: Dr Braunwald in the Early 1970s



Achievements

My name appears on about 1,700 publications in cardiovascular and general medical journals, but this is not something I am particularly proud of. It is not the quantity that counts, it is the quality. When I think about my research, I divide it into one major and three minor achievements.

Time is Muscle

My major achievement can be summed up in the phrase 'time is muscle'. It started with a eureka moment at the NIH. It had long been assumed that MI results from a blood clot in a coronary artery, which suddenly causes necrosis of the muscle perfused by this artery, akin to turning off a light switch. However, something I observed led me to challenge that assumption. I saw the ECG of a patient with acute myocardial infarction showing changes that seemed to be associated with changes in blood pressure, which occurred over the course of several hours. I suspected there might be interventions that could be carried out in patients experiencing MI. The development of an infarction was comparable to a rheostat that could be turned up or down slowly, as opposed to a binary light switch.

When I got to UC San Diego, my colleagues and I began experiments in anaesthetised dogs that proved the size of – and damage done by – MI could be reduced after the initial obstruction. We showed that early reperfusion was key and the longer the heart is ischaemic, the more heart muscle dies. These experiments were performed before coronary angioplasty had been developed but, once this new technique was popularised, the concept of infarct size limitation was applied successfully to many patients.

In 1984, I founded the Thrombolysis In Myocardial Infarction (TIMI) Study Group, an academic research organisation at the Brigham. We have run more than 60 clinical trials and have branched out from the original mission to include heart failure and the influence of diabetes on the heart.

My minor achievements fall into three related categories – hypertrophic cardiomyopathy, heart failure and cholesterol.

Hypertrophic Cardiomyopathy

The first of my minor achievements is the understanding and treatment of hypertrophic cardiomyopathy. Glenn Morrow and I recognised this as a unique clinical entity in 1959. We came to understand that it is often an inherited condition. It can be benign, but it can also cause ventricular arrhythmias and sudden cardiac death in young people, especially those engaged in vigorous sports. This is why high school and college students should undergo a cardiac examination before going out for football and other physically demanding activities.

We showed how beta-blockers can help these patients and Morrow developed a successful operation, ventricular myectomy, which is known as the Morrow procedure. Both of these treatments are still widely used.

Heart Failure

My next achievement is in the area of heart failure, a condition I consider to be the price we pay for success. We now know how to treat patients with acute MI and valvular or congenital heart diseases, but typically we cannot cure these conditions. Instead, we prolong patients' lives, often for as long as 20 or 30 years. However, eventually, their hearts may fail. In fact, heart failure is now the most common diagnosis in hospitalised patients on Medicare.

In 1962, when I was at the NIH, we first described a technique that measures how well the ventricles are pumping blood with each beat. This measurement is known as the ejection fraction and it is now used on most patients suspected of having heart failure.

Years later in the late 1970s at Harvard and the Brigham, my colleague Marc Pfeffer and I showed that an angiotensin-converting enzyme inhibitor prolonged life in patients whose ejection fraction had fallen after a myocardial infarction.

I am still actively involved in heart failure and we continue to look at new medications. In fact, we have recently finished a trial that showed a new drug, sacubitril/valsartan, is safe and effective in patients hospitalised with acute, decompensated heart failure.

Cholesterol

We now know that an elevated level of circulating LDL cholesterol is the most important risk factor for the development of atherosclerosis. My colleagues and I have carried out a series of clinical trials showing that the lower the circulating level of LDL cholesterol, the lower the risk of MI or stroke. Initially, experts were aiming for LDL cholesterol levels below about 3.11 mmol/l. This was later reduced to 2.33 mmol/l. However, we have now shown there may be beneficial effects under 1.30 mmol/l; a concentration once considered to be outrageously low. My colleagues in TIMI have evidence that you can lower LDL cholesterol to <0.52 mmol/l without any apparent ill effects.

Textbook Editing

Another of my most gratifying activities has been my work as an editor of two textbooks. The first is on internal medicine (*Harrison's Principles of Internal Medicine*). I have had the opportunity to serve as an editor of 12 editions and an editor-in-chief of two of them. In 1980, I decided to edit a textbook of cardiology (*Braunwald's Heart*

Disease), which has completed 11 editions. Both of these books remain popular among trainees worldwide.

Ringside Seat

It has been more than 80 years since that dark day in Vienna when everything changed. Nina died in 1992, but my three daughters (Karen, a clinical psychologist; Allison, a physician; and Jill, a lawyer), bring me joy, as do my seven grandchildren and two great-grandchildren. My second wife, Elaine, was a hospital executive. She is supportive and a great companion.

My days are full. I usually get up at around 7 am, work at home for a while, drive to the hospital and meet with trainees and cardiology fellows to go over their work. I spend a lot of time writing and editing and I attend clinical conferences at the Brigham regularly.

My interest in cardiology began 68 years ago when I was a medical student. I have been privileged to have a ringside seat to the enormous life-prolonging advances in this speciality. While this progress represents a great triumph, there is still much to be done in the field. ■