

## Facts and ideas from anywhere



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### LIFE LESSONS FROM MODERN-DAY GREATS IN CARDIOVASCULAR DISEASE

Beginning in July 1996, interviews of prominent cardiovascular specialists began appearing in *The American Journal of Cardiology* (AJC). Shown in *Table 1* are the names of the 62 cardiovascular internists whose interviews have been published in the AJC. One interview was done by

Dr. Mark Silverman, two by Dr. J. Willis Hurst, one by Dr. Charles Stewart Roberts, one by Dr. Colin Ku Lo Phoon, and the others by me. Three interviews focused on a medical topic rather than on the interviewee, and they are not considered further in this discussion. Interviews of eight cardiovascular surgeons also have appeared in the AJC, and their names are listed in *Table 2*.

In addition to the 70 interviews in the AJC, 73 others (interviewed by me) have been published in *Baylor University Medical Center Proceedings* (*Table 3*), but they are not considered further in this piece.

Certain data on the 59 cardiovascular internists (personal interviews) and on the 8 cardiovascular surgeons (total 67) are shown in *Table 4*. Their ages at the time of their interviews averaged 65 and 74 years, respectively. Most were born between 1926 and 1950. Eleven (17%) were born outside the USA. Of the 52 internists who grew up in the USA (one of whom was born abroad), 26 (50%) grew up in the Northeast, mostly in New York City (15 of 26); 11 grew up in the US's midportion; 15%, in the Southeast; and 14%, in the West. Seven of these 67 had no siblings. Of those with siblings, the interviewees were most often the first child (over 50%). In 10 (15%) of the 67 interviewees, a parent had died when the interviewee was <20 years of age. Over half played on one or more high school athletic teams and well over 20%, on college varsity teams. The interviewees had an average of 2.7 and 3.1 children, respectively. Ten (17%) of the 59 cardiovascular internists and none of the 8 cardiovascular surgeons were divorced. The first publication was at a relatively early age, mean 29, and the range was 23 to 36 years. (That finding is of interest since

**Table 1. Interviews of cardiovascular medicine specialists published in *The American Journal of Cardiology* (1996–2008) (n = 62)**

Eric Jeffrey Topol	Carl John Pepine
James Thornton Willerson	Kenneth Hardy Cooper
Joseph Stephan Alpert	Watkins Proctor Harvey
John Willis Hurst*	Joseph Kayle Perloff
Jesse Efreem Edwards	Charles Richard Conti
Howard Bertram Burchell	William Watts Parmley
William Howard Frishman	Dean Michael Ornish
Robert Ogdon Bonow	Dean Towle Mason
Eugene Braunwald	George Allan Beller
Joseph Cholmondeley Greenfield	Leslie David Hillis
Norman Mayer Kaplan	Douglas Peter Zipes
Robert McKinnon Califf	Nanette Kass Wenger
Bernard John Gersh	Andrew Peter Selwyn
Dean James Keriakes	Arthur Garson, Jr.
Jeffrey Michael Isner	Edward David Frolich
Scott Montgomery Grundy	Robert Alan Vogel
Burton Elias Sobel	Ferid Murad
Robert Anthony O'Rourke	Steven Evan Nissen
Spencer Bidwell King III	William Peter Castelli
Robert Roberts	Wallace Bruce Fye III
Eugene Austin Stead, Jr.†	Anthony Nicolas DeMaria
Bertram Pitt	Barry Lewis Zaret
Christopher John Dillon Packard¶	Franz H. Messerli
Terje Rolf Pedersen¶	Joseph Lascalzo
Valentin Fuster	Donald Carey Harrison
Henry Arthur Solomon	Hollis Bryan Brewer
Harvey Stanley Hecht¶	Barry Joel Maron
Myrvyn Harold Ellestad	William Clifford Roberts§
Richard John Bing†	Jean Schlatter Kan‡
Melvin Mayer Scheinman	Robert William (Bobby) Brown
James Stuart Forrester III	Lawrence Cohen

\*Interviewed by Mark Silverman.

†Interviewed by John Willis Hurst.

‡Interviewed by Colin K. L. Phoon.

§Interviewed by Charles S. Roberts.

¶Topic interviews.

**Table 2. Interviews of cardiovascular surgeons published in *The American Journal of Cardiology* (1997–2006)**

Michael Ellis DeBakey
Denton Arthur Cooley
John Webster Kirklin
David Coston Sabiston, Jr.
David Kempton Cartwright Cooper
Francis Robicsek
Magdi Habib Yacoub
Lawrence Harvey Cohn

now the age of those receiving their first National Institutes of Health research grant is 42 years.) All of these interviewees were highly productive, and 43% had over 500 publications in medical journals. A number were president of the American Heart Association or the American College of Cardiology, and 7 of the surgeons were president of one or more national surgical organizations. About a third of their mothers worked, and also a third of the spouses worked. Seven were married to physicians but only two of those spouses practiced medicine. Less than a third were overweight. Six had a PhD in addition to an MD. Of the 59 cardiovascular internists, 24 (41%) were Jewish, as was one of the 8 cardiovascular surgeons. Of the 54 cardiovascular internists who attended college or medical school or did training in the USA, just over half had some training at an Ivy League university or medical center. (Ivy League, however, does not include such institutions as New York University, Johns Hopkins, or any school in the South, Midwest, or West.) None of these 67 interviewees could be considered heavy alcohol users.

Some characteristics of the parents of the 67 interviewees are shown in *Table 5*. One or both of 25 (37%) couples were born outside the USA; in 42 (63%) one or both parents attended college; in 8 of the 67 couples, one or both were physicians; only 2 (3%) were divorced; the average number of children was 2.8; and the interviewee was an only child in 8 (12%).

The major commonalities among these 67 interviewees are summarized in *Table 6*. Without exception, the parents were devoted to their children, love was abundant in their homes, education was incredibly stressed by their parents, the home atmosphere provided an enormous curiosity to learn, nearly all were superb students, all had a passion for medicine, and all worked exceedingly hard. Most slept <6 hours per night, and all were incredibly focused on their goals. Writing was a major priority, and they all worked hard at it. Most were good teachers and good mentors. In my view, all were very competitive. They had strong character. Most had a good capacity for friendship, alcohol played little to no major role in their lives, and most maintained healthfulness.

I have reproduced small portions from two interviews: that of Dr. Eugene Braunwald (1), the most renowned cardiologist in the 20th century, and that of Dr. Michael E. DeBakey (2), the most renowned cardiovascular surgeon in the past century.

**Table 3. Interviews by WCR published in *Baylor University Medical Center Proceedings***

<b>Baylor physicians</b>	
Lloyd Wade Kitchens, Jr.	Robert Peter Perrillo
David Joseph Ballard	David Wesley Barnett
Adrian Ede Flatt	George Kennedy Hempel, Jr.
J. B. Howell	Joseph Allen Kuhn
George Justice Race	Virginia Pascual
Michael Emmett	William Mark Armstrong
Marvin Jules Stone	William Levin Sutker
Ronald Coy Jones	Perry Edward Gross
Jimmie Harold Cheek	Barry Wayne Uhr
Robert Wilson Jackson	Carolyn Michelle Matthews
<b>Baylor nonphysicians</b>	
George Marion Boswell, Jr.	Luz Remedios Tolentino
Göran Bo Gustaf Kintmalm	Boone Powell, Jr.
Robert Pickett Scruggs III	Joel Tribble Allison
Wilson Weatherford	Mark Timothy Parris
Fred David Winter, Jr.	Gary Dale Brock
Gary L. Davis	Julie Michelle O'Bryan
Peter Allen Dysert II	Herman Grant Lappin
Zelig ("Zeck") Lieberman	Albert Julio Alvarez
Martin Alan Menter	
Harold Clifton Urschel, Jr.	
<b>Visiting professors</b>	
John Flake Anderson	Gerald Bernard Appel
John W. Hyland	Robert William Schrier
Joyce Ann O'Shaughnessy	Larry Harold Hollier
Daniel Earl Polter	Charles Stone Bryan
Jonathan Martin Whitfield	Richard Vaile Lee
Andrew Zolton Fenves	Gregory Gordon Dimijian
Glenn Weldon Tillery	Peter Emanuel Dans
Clement Richard Boland, Jr.	Donald Wayne Seldin
Elmer Russell Hayes	Ellen Taylor Seldin
Robert Lee Fine	Thomas John (Jock) Murray
Jay Donald Mabrey	Matthew Whitfield Ridley
Donald Alan Kennerly	Robert Ogden Bonow
Barry Cooper	David Westfall Bates
Robert Gary Mennel	Robert Steven Galvin
Paul Bernard Convery	Carolyn Maureen Clancy
Irving David Prengler	Lynne Anne Marcum Kirk
Zaven Hogop Chakmakjian	Lee Marshall Nadler
Priscilla Larson Hollander	

**Eugene Braunwald, MD (1929–)**

Dr. Braunwald was born on August 15, 1929, in Vienna, Austria, and lived his first 9 years there.

**Roberts:** *Can you discuss your life in Vienna?*

**Braunwald:** My memory of that period falls into two very distinct phases: before and after March 13, 1938. On that date

**Table 4. Data on the interviewees**

Variable		Internists (n = 59)	Cardiovascular surgeons (n = 8)	Variable		Internists (n = 59)	Cardiovascular surgeons (n = 8)
Age of interviewee (years)		41–91 (mean, 65)	59–88 (mean, 74)	Divorced		10 (17%)	0
Year of birth				Age (years) at first publication		24–36 (mean, 29)	23–34 (mean, 29)
1901–1925		9 (15%)	5 (63%)	Publications in medical journals**			
1926–1950		45 (76%)	3 (37%)	<250		15/58 (26%)	1 (12%)
1951–1954		5 (8%)	0	251–500		19/58 (33%)	2 (25%)
Country of birth				>500		24/58 (41%)	5 (63%)
USA		51 (86%)	5 (63%)	President of the American Heart Association or the American College of Cardiology or a major surgical society		21 (36%)	7 (88%)
Non-USA		8 (14%)	3 (37%)	Mother worked		21 (36%)	2 (25%)
State grew up in				Spouse worked		19 (32%)	2 (25%)
NE 26/52 (50%)	New York	15*		Married a physician		5 <sup>†</sup> (8%)	2 <sup>†</sup> (25%)
	Pennsylvania	4		Overweight		19 (32%)	2 (25%)
	Connecticut	1		PhD		5 (8%)	1 (12%)
	New Jersey	4		Jewish		24 (41%)	1 (12%)
	Massachusetts	1		Ivy League education <sup>‡</sup>			
	Maryland	1		College		13/54 <sup>§</sup> (24%)	0
Mid-US 11/52 (21%)	Indiana	1		Medical school		12/54 (22%)	1/5 <sup>†</sup> (20%)
	Ohio	4		Houseofficership		11/54 (20%)	1/5 (20%)
	Minnesota	0	1	Fellowship		15/54 (28%)	0
	Oklahoma	2		At least 1 of the 4		28/54 (52%)	2/5 (40%)
SE 8/52 (15%)	Texas	4	1	Drinks alcohol			
	Virginia	1		None		6 (10%)	1 (12%)
	Georgia	4		Drinks wine at a social event		16 (27%)	0
	South Carolina	1		Usually daily wine		24 (41%)	0
West 7/52 (13%)	North Carolina	0	1	Spirits		7 (12%)	6 (75%)
	Louisiana	1	1	Uncertain		6 (10%)	1 (12%)
	Alabama	1					
	California	5	1				
Wyoming	1						
Utah	1						
Number of siblings							
None		5 (8%)	2 (25%)				
1–5		54 (92%)	6 (75%)				
Hierarchy of interviewees in the families with >1 child							
First child		29/54 (54%)	3/6 (50%)				
Last child		12/54 (22%)	2/6 (33%)				
In between		12/54 (22%)	1/6 (17%)				
A parent died when interviewee ≤20 years old		8 (14%)	2 (25%)				
Competitive athlete							
High school only		31 (53%)	7 (88%)				
College also		13 (22%)	5 (63%)				
Children		157 (2.7)	25 (3.1)				
0		2 (3%)	1 (12%)				
1		2 (3%)	0				
2		23 (39%)	1 (12%)				
3		21 (36%)	3 (38%)				
4		9 (15%)	1 (12%)				
5		2 (3%)	2 (25%)				

\*One was born outside of the USA but grew up in New York City.

\*\*One interviewee who was not in academia was excluded.

<sup>†</sup>Only 1 practiced medicine.

<sup>‡</sup>Brown, Columbia, Cornell, Dartmouth, Harvard, Princeton, University of Pennsylvania, Yale. Does not include New York University, Johns Hopkins, or any school in the South, Midwest, or West.

<sup>§</sup>The other 5 had all their training abroad.

<sup>††</sup>The other 3 had all their training abroad.

the Nazis occupied Austria in the so-called *Anschluss*. My childhood was idyllic before that. We lived in one of the elegant areas of Vienna. I went to an excellent school and had private tutors in English and piano. My parents were very interested in opera, and by the time I was 6 they had begun taking me to the Vienna State Opera. Vienna was a gracious city in the 1930s, the cultural capital of central Europe. Then, suddenly, on March 13, 1938, everything changed. I recall vividly the enthusiastic crowds welcoming Hitler and his troops marching into Vienna. My father's and other Jews' businesses were taken over

**Table 5. Data on the parents of the 67 interviewees**

Variable	N	% or mean
One or both born in a non-USA country	25	37%
Attended college (1 or both)	42	63%
Were physicians (1 or both)	8	12%
Divorced (after interviewee was born)	2	3%
Number of children	188	2.8
1 (interviewee)	8	12%
2	24	36%
3	18	27%
4	9	13%
5	6	9%
6	2	(3%)

**Table 6. Commonalities among interviewees**

Parents devoted to children
Love abundant from parents
Education stressed by parents
Enormous curiosity to learn
Superb students
Passion for medicine
Worked exceedingly hard
Slept little (<6 hours)
Incredibly focused on goals
Good writers
Good teachers and mentors
Competitive
Strong character
Good capacity for friendship
Little or no alcohol
Maintained healthfulness

imity of our apartment to his business allowed him to have lunch with us quite frequently. In childhood, both of my parents had been too poor to receive an education beyond high school. My father was fifth-generation Viennese, and my mother was born in a small town in the east of what was then the Austro-Hungarian empire. Her family fled to Vienna at the end of World War I because of an anti-Jewish pogrom in her town. My father had built a successful wholesale clothing business by the time I was born, and we enjoyed a very pleasant life. The three most important things that I learned from those early years were a central focus on the well-being of the nuclear family, a reverence for learning, and an interest in classical music. As I just mentioned, we lived not far from the University of Vienna, and when I was 6 or 7 years old my mother took me for walks in the Stadtpark adjacent to the university. She would point to the

several days later and their liquidation was begun. We lived in constant terror from March until the end of July 1938, when we escaped from Austria. Many people in our situation, of course, did not escape.

**Roberts:** *Before March 13, 1938, you lived next to your father's business? What was your father like? Your mother? What were your day-to-day activities, not only at school, but at home in those more pleasant moments?*

**Braunwald:** Our apartment was just off the Schottenrink, Vienna's major thoroughfare, close to the university and to the state opera. I saw a good deal of my father because the proximity

of our apartment to his business allowed him to have lunch with us quite frequently. In childhood, both of my parents had been too poor to receive an education beyond high school. My father was fifth-generation Viennese, and my mother was born in a small town in the east of what was then the Austro-Hungarian empire. Her family fled to Vienna at the end of World War I because of an anti-Jewish pogrom in her town. My father had built a successful wholesale clothing business by the time I was born, and we enjoyed a very pleasant life. The three most important things that I learned from those early years were a central focus on the well-being of the nuclear family, a reverence for learning, and an interest in classical music. As I just mentioned, we lived not far from the University of Vienna, and when I was 6 or 7 years old my mother took me for walks in the Stadtpark adjacent to the university. She would point to the

university and say to me, "You will be a professor there someday." Because my parents had been deprived of an education themselves, they made my education their highest priority.

**Roberts:** *Did you have intellectual discussions at the dinner table at night or at lunch time?*

**Braunwald:** I remember discussions of history, economics, and politics at the dinner table. My parents probably did emphasize such discussion because of their own lack of higher education. Of course, there was much talk about music. Actually, my parents had met in the standing room area at the Vienna State Opera!

**Roberts:** *Although your parents were poor initially, your father became quite successful?*

**Braunwald:** Yes. By the time of the *Anschluss* he had a prosperous business, but the Nazis quickly sent SS officers to liquidate all Jewish businesses. The officer who was assigned to my father's business had, I believe, been imprisoned for the assassination of Chancellor Dollfuss of Austria several years earlier. I got to know this SS officer because sometimes he came over to the apartment for lunch or coffee.

**Roberts:** *What was he like?*

**Braunwald:** He was cold and businesslike but always polite as he went about destroying our livelihood. The liquidators themselves were able to make off with most everything, and therefore he wanted the process to be rapid and complete.

**Roberts:** *How did it come about that your father was arrested by the Nazis within a couple of months of their invading Austria?*

**Braunwald:** It was the proverbial knock on the door in the middle of a night in May 1938. I remember being awakened by my parents at about 3:00 AM. My mother was hysterical, screaming, "They are taking your father away!" He had 15 minutes to get dressed and to say goodbye to us. I now recall that he was remarkably stoic about it. Then my mother, my younger brother, and I ran to the window and saw him herded into an open truck with 15 or 20 other men. They were then driven off to the railroad station.

**Roberts:** *How did your mother get him back? I gather he came back the next day?*

**Braunwald:** Yes. It is incredible what life can hinge on. When "our" SS officer came to the business the next morning, he asked for my father. My very upset mother said he had been taken away, presumably to a work camp. He shrugged his shoulders. (My mother and I subsequently talked about this event innumerable times.) Then came the pivotal moment. She said something along the following: "You need him back because you have liquidated only half of the business, and if you get him back you can liquidate the rest. Look how much richer you would be." He replied, "You might be right." He then phoned the depot to find that my father was about to board the train. My mother only overheard his side of this conversation in which he pulled rank on the officer at the depot, saying, "I don't care if you are a full colonel in the German army, I am a captain in the SS and I want this Jew returned!" So it ultimately became a matter of authority. By 11:00 AM my father was returned to us. He had been gone for only 8 hours, but it was a very close call. If my mother had not acted at that moment, none of our

family would have survived, and of course, we wouldn't be having this interview.

**Roberts:** *From that point it was about 2 months before you escaped? What happened in the interim?*

**Braunwald:** My father had actually begun preparations for our escape in March immediately after the occupation, but he redoubled his efforts after his brief arrest. There were several opportunities for him to leave Vienna alone and to try to bring us along later, but he refused to allow the family to be separated. He insisted that we stay together even though that made escape more difficult. But he obviously calculated correctly. We left at the end of July 1938, in something that resembled the *Sound of Music* story, except that there was no music. We ended up in London, totally destitute, literally with only the shirts on our backs. We were taken care of by a relief agency. I spoke a little English because of the special tutoring I had received, but my parents did not then speak a word of English. (They later learned English in night school.) . . .

### Michael Ellis DeBakey, MD (1908–2008)

**Roberts:** *What was it like growing up in your family and in Lake Charles, Louisiana?*

**DeBakey:** First, Bill, I was blessed with parents who were both highly intelligent and exceedingly kind and generous in their temperament and psyche. They lived almost exclusively for their children. They wanted to give us the best of everything, and they believed education was crucial. They were both first-generation immigrants, having come to this country as children. Because they believed that a good education was essential to prepare us for a fulfilling life, they always encouraged us to excel in our studies. For example, they urged us to go to the local library once a week and choose any book we wanted to read. We had a small but very good library in Lake Charles. I came home from the library one day and told my father that there was a wonderful set of books there, but you could not borrow them; you had to read them in the library. He asked me the name of the book, and I responded, *The Encyclopaedia Britannica*. He said, "Well, we will get it." I don't remember how many volumes there were at that time—not as many as there are today—but he purchased the complete set. All of us, my brother, sisters, and I, before we went to college, had each read that whole set of *The Encyclopaedia Britannica*. That is how important it was to us, not only from an educational standpoint, but mainly because we enjoyed reading.

All of us excelled at school; we all led our classes. My sisters all led their classes. They were smarter than I was; at least they were a little more studious. My brother and I wanted to play and do other things. The one thing that I never got an A in was deportment. In those days we had a deportment grade, and I had great difficulty with it because I would finish all my studies and would get bored because the teacher was dealing with material I had already mastered.

In what we then called grammar school or elementary school—I think I was in the fifth or sixth grade—the classes were divided into two sections, A and B, and the same teacher taught both classes. While she was teaching one class, she would

give the other class a study period of 30 minutes, after which she would go back to the other side. She noticed I was sitting in the center, paying attention to what she was doing, whether she was in my class or the other one. So near the end of the class, she said to me one day, "I notice that you are paying attention to both classes. Would you like to take the exam for both of them?" I said, "Sure." I took both exams and was permitted to skip a grade because I passed the exam.

School was fun for me because I enjoyed learning new things. My parents had always emphasized to all of us the joy of learning. I studied, learned, and earned good grades, and I think that became a habit.

**Roberts:** *Did your parents go to college?*

**DeBakey:** No, but they were self-educated, read widely, and had remarkably critical minds and retentive memories.

**Roberts:** *And they pushed education to the hilt.*

**DeBakey:** Yes, absolutely.

**Roberts:** *I presume you read the book or books that you got from the library once a week?*

**DeBakey:** Yes, regularly.

**Roberts:** *From age 6 through age 17, I calculate that you must have read over 600 books outside of school.*

**DeBakey:** Yes, at least, plus the encyclopedia. I was a voracious reader. In fact, we had to go to bed at a certain time. We would do our lessons—our parents would make sure we had done our lessons—and then if we had time, we would read the library book or sections of *The Encyclopaedia Britannica*. Often, we were all going to *The Encyclopaedia Britannica* at the same time. Of course we would not read the same thing. Usually by 10:00, our parents wanted us in bed, because we had to get up early. Our father was a very early riser, and we all had assigned chores to encourage self-discipline and responsibility, even though my parents had a house staff. By 5:00 AM we were up. I guess I got habituated to the early rising.

That came in handy, because when I first started as a freshman in college, I lived in a dormitory, and the boys were raising cane all night. I wanted to study but couldn't because of the commotion. I would just go on to bed and get up at 3:00 or 4:00 AM and do all my studying while it was quiet. So I got into the habit of getting up early, and it does not matter what time I go to bed now; I still arise at 5:00 AM. I read *The New York Times* and *The Wall Street Journal* in about 30 minutes. After that I can get some of the things done that I may not be able to do during the day—work on a manuscript or attend to some other paperwork. Getting up early has been of great value not only in my surgical practice but also in allowing me an additional couple of hours beyond that of the average person. Fortunately, I manage well on 5 or 6 hours of sleep a night, just as my father did.

**Roberts:** *So if you get 5 hours of sleep a night and you are 88 years old, you have slept only 14 of your last 68 years?*

**DeBakey:** You are probably right about that. If you sleep 8 hours a night (one third of every day) and you live 60 years, you have really lived only two thirds of that time, or 40 years. So whatever you can take from your sleep extends your conscious living.

**Roberts:** So you are 88 years and a maximum of one fifth of your life has been spent sleeping.

**DeBakey:** That is about right. And that gives me a tremendous advantage. People ask me, “How in the world could you write nearly 1500 articles in that period of time?” If you live your life long enough and you have enough time, you can do it.

**Roberts:** Yes, but you don't waste a minute. You spend very little time commuting. You live 5 minutes from the hospital.

**DeBakey:** In fact, I deliberately chose to live near the college. When I first came to Houston, I rented a house that was also only about 10 minutes from here. . . .

## FIFTY YEARS OF HYPERTROPHIC CARDIOMYOPATHY\*

In 1869, Liouville (3) and Hallopeau (4) each reported a patient probably having hypertrophic cardiomyopathy (HC). Both authors noted striking hypertrophy of the ventricular septum, and each considered the left ventricular outflow tract to be obstructed by the hypertrophied septal muscle; Hallopeau noted thickening of the anterior mitral leaflet in his 69-year-old patient.

In 1907, Schmincke (5) described severe hypertrophy of the ventricular septum in the hearts of two women aged 50 and 56 years. In addition to the septal thickening, the left ventricular free wall in each patient was severely hypertrophied. Schmincke considered the ventricular septal hypertrophy to be primary and of congenital origin, leading to obstruction to left ventricular ejection and to secondary hypertrophy of the left ventricular free wall.

After Schmincke's report in 1907, a period of nearly 50 years elapsed before another probable report of this disease appeared. In 1952, Davies (6) described a family in which many members had heart disease and a history of sudden death and systolic precordial murmurs. At necropsy, the heart in one patient showed “diffuse sub-aortic stenosis” associated with left ventricular hypertrophy. He described an area of fibrosis 4 cm square in the left ventricular outflow tract opposite the anterior mitral leaflet, a lesion highly suggestive of HC.

In 1957, Brock (7) operated on a 63-year-old woman thought to have a valvular aortic stenosis and systematic hypertension. At operation, however, the aortic valve was normal, and no obstruction to left ventricular outflow was encountered by dilating instruments despite direct pressure tracings showing subvalvular obstruction. The patient died shortly after operation, and necropsy showed a hypertrophied, nondilated left ventricular cavity and no subaortic fibrous stricture.

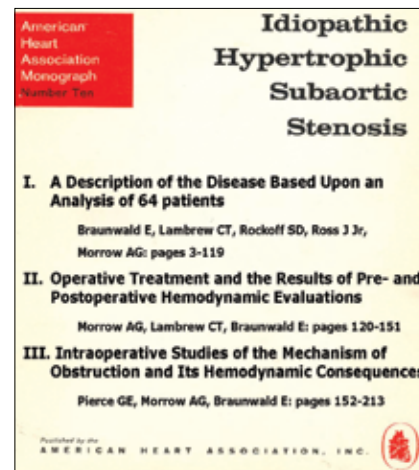
Although the cases reported by Liouville (3), Hallopeau (4), Schmincke (5), Davies (6), and Brock (7) are probable examples of HC, the comparative thickness of the ventricular septum and left ventricular free wall were not described in any of them. The first unequivocal description of HC was by Teare (8) in London, reported in the *British Heart Journal* in January 1958. Although Brock's clinical report was published in *Guy's Hospital Reports* in the final quarterly issue of 1957, Teare's paper had been received by the journal in January 1957—that is, *before* Brock had operated on his patient—and Brock's publication did not

appear until 1958, although the date on the issue was 1957. Thus, it is fair to credit Teare with the first detailed anatomic description and credit Brock with the first description of the functional nature of this entity.

Teare described gross and histologic cardiac findings in 9 patients (aged 14 to 45 years [average 26]); 2 women, 7 men), 8 of whom died suddenly. Although he did not give measurements of the thicknesses of the ventricular septum and left ventricular free wall, he clearly indicated and illustrated that the septum was thicker than the left ventricular free wall and, indeed, called the condition *asymmetrical hypertrophy of the heart*. He considered the localized septal hypertrophy to be a “benign tumor” or “hamartoma.” He observed on histologic examination “bizarre arrangements of muscle bundles” and “considerable variation in size” of the myocardial fibers in the ventricular septum. He also noted similar disordered arrangement of muscle bundles in the adjacent anterior free wall of the left ventricle. In one patient the posterior left ventricular free wall “appeared thinner than normal,” and histologic examination of it showed normal arrangement and uniform size of the myocardial fibers. Although one of his 9 patients underwent valvulotomy for suspected mitral stenosis (this was the only patient in his study who had not died suddenly), there were no descriptions of the mitral valve, no mention of mural endocardial thickening in the left ventricular outflow tract, and no comments regarding the sizes of the various cardiac chambers. This report, however, established HC as a distinct entity.

Although these heretofore mentioned reports, mainly necropsy ones, are likely examples of the disease, HC was put on the clinical screen by Braunwald and his colleagues in 1960 (9), and, by 1964, Braunwald and colleagues (10–12) reported extensive clinical and operative studies on 64 of these patients (*Figure 1*). This American Heart Association monograph included 213 pages of original work! No condition in the annals of medicine had been described so extensively in such a short period of time, and Dr. Braunwald deserves the credit. Indeed, as Dr. William Osler emphasized: “In science the credit goes to the man who convinces the world, not to the man to whom the idea first occurred.”

\*A modified version of this piece was presented on October 4, 2008, at the Scientific Symposium sponsored by the Eugene Braunwald Endowment for the Advancement of Cardiovascular Discovery and Care at the Brigham and Women's Hospital in Boston, Massachusetts.



**Figure 1.** The 1964 monograph of 213 pages by Braunwald, Morrow, and colleagues.

**Table 7. Hypertrophic cardiomyopathy: cardiac findings divided by presence or absence of cardiac operation**

Characteristic	Cardiac operation		Totals (n = 230)
	0 (n = 153)	+ (n = 77)	
Dilated atria	98%	100%	99%
Increased heart weight	95%	96%	96%
Nondilated left ventricle	82%	75%	80%
Thickened anterior mitral leaflet	66%	94%	75%
Mural plaque, LVOT	60%	93%	71%
Ventricular septum > left ventricle	71%	63%	68%
Transmural scarring, VS and/or LV wall	42%	43%	42%
Disorganization, cardiac myocytes	95%	95%	95%
Intramural coronary disease	83%	83%	83%
Interstitial fibrosis, VS and LV wall	90%	90%	90%

LV indicates left ventricular; VS, ventricular septum; LVOT, left ventricular outflow tract.

Dr. Albert Schweitzer opined, “As we acquire more knowledge, things do not become more comprehensive, but more mysterious.” Certainly this statement is applicable to HC as it has unfolded in the last 50 years.

Shown in *Table 7* are morphologic features of 230 patients with HC studied at autopsy by the same individual from 1959 to the present time (13). The diversity of anatomic findings has altered the definition of this condition on several occasions. Essentially, none of the 10 morphologic features occurs in all patients. The ventricular septum is thicker than the left ventricular free wall in about two thirds of the patients, not 100% as some originally thought. Cardiac mass is usually—but not always—increased (14). This condition has produced the largest hearts known to humankind (15).



**Figure 2.** Hearts with hypertrophic cardiomyopathy from two 15-year-old boys who died suddenly. The heart on the left weighed 1415 g, and the ventricular septum was much thicker than the left ventricular free wall. The heart on the right weighed 425 g, and the thicknesses of both ventricular septum and left ventricular free wall were similar.

**Table 8. Hypertrophic cardiomyopathy: gross cardiac findings by three age groups in 153 patients without a cardiac operation**

Characteristic	Age group (years)		
	≤10 (n = 15)	11–70 (n = 124)	>70 (n = 14)
Dilated atria	95%	100%	100%
Increased heart weight	80%	98%	86%
Nondilated left ventricle	73%	81%	93%
Thickened anterior mitral leaflet	27%	66%	100%
Mural plaque, LV outflow tract	27%	78%	100%
Ventricular septum > left ventricle	73%	71%	79%
Transmural scarring, VS and/or LV wall	0%	45%	50%

LV indicates left ventricular; VS, ventricular septum.

*Figure 2* shows the hearts of two 15-year-old boys with HC (16). Both died suddenly. The heart on the left weighed 1415 g, the heaviest I have ever seen. The ventricular septum was much thicker than the left ventricular free wall. The heart on the right weighed 425 g, or 30% of the one on the left. The ventricular septum and left ventricular free wall were of similar thickness. Yet, both had the same condition, namely HC.

The congenital condition—according to Dr. Barry Maron—is present in 1 of 500 humans, the same prevalence, incidentally, as that of familial hyperlipidemia (17, 18). It can be manifested in newborns or not until the nonagenarian age group (*Table 8*) (17, 19). It is, of course, a congenital heart disease that usually is not manifested until adulthood (20).

HC has many complications, and some are listed in *Table 9*. Sometimes a complication is the first clinical manifestation of the condition.

**Table 9. Hypertrophic cardiomyopathy: complications**

1. Death: sudden and nonsudden
2. Atrial dilatation: atrial fibrillation
3. Mitral valve disease: mitral regurgitation
  - A. Fibrous thickening (anatomic systolic anterior motion)
  - B. Insertion, papillary muscle, into leaflet
  - C. Rupture of chordae tendineae
  - D. Prolapse
  - E. Annular calcification
  - F. Infective endocarditis
  - G. Papillary muscle calcification
4. Myocardial infarction: left ventricular dilation
5. Left ventricular apical diverticulum
6. Pulmonary hypertension
  - A. Aneurysm pulmonary arteries
  - B. Ossific nodules, lungs
7. Heart block and bundle branch block



**Figure 3.** Heart of a patient who had partial ventricular septectomy and septotomy for hypertrophic cardiomyopathy. Both the septal mural endocardium and the anterior mitral leaflet were thickened by fibrous tissue. The thickening represents the anatomic equivalent of systolic anterior motion of the anterior mitral leaflet.

*Figure 3* shows a heart in which the myectomy-myotomy procedure had been performed. The operation was devised by Dr. Andrew G. Morrow (11), who performed 299 of these operations and who himself had the disease. This operation is not for the occasional heart surgeon, and that is one reason I predict that it will eventually vanish. Mitral valve replacement is not the proper operation except in patients with very damaged mitral valves from infective endocarditis (21, 22).

*Figure 4* shows a HC heart in a patient who developed extensive ventricular septal scarring with ventricular cavity dilation, an occurrence, according to Dr. Barry Maron, of 2% of these patients (23). These patients are candidates for cardiac transplantation (24).

In summary, HC was put on the diagnostic and therapeutic map by Dr. Braunwald and his colleagues in the early 1960s. Much additional information, of course, has been learned subsequently. This condition produces the largest myofibers of any condition with or without the stimulus of ventricular outflow obstruction or elevation of ventricular peak systolic pressures. The ultimate therapy, in my view, will involve an agent that reduces myofiber size. Whether myofiber number is increased in HC remains unclear.

#### FORTY-FIVE YEARS IN THE CARDIOVASCULAR ARENA

In 1963 I was a cardiology fellow under Drs. Eugene Braunwald and Andrew G. Morrow in the National Heart Institute of the National Institutes of Health in Bethesda, Maryland. That was the year that President John F. Kennedy was killed in Dallas, Texas. When he arrived at Parkland Hospital there was no electrocardiographic machine in the emergency room (25). What has occurred in cardiovascular medicine since that fatal November day in 1963 is astounding! No specialty in medicine has had such a transformation.

In 1963 a patient with acute myocardial infarction (AMI) was treated about the same as when my father had his first heart attack in 1938, 25 years earlier. It was bedrest on the ward or in a private room, and that went on for a month. In 1963, there were no coronary care units, no echocardiograms, no intravascular ultrasonic imaging, no myocardial perfusion imaging (nuclear cardiology), no computed tomography, and no magnetic resonance imaging. Coronary angiography was being done in only three or four hospitals in the entire USA. And, of course, there was no coronary angioplasty or coronary



**Figure 4.** Transverse slice of the cardiac ventricles in a 46-year-old man with hypertrophic cardiomyopathy who developed extensive ventricular septal scarring and dilatation of both ventricular cavities. The resulting severe heart failure prompted cardiac transplantation. Reproduced with permission from Shirani et al, 1993 (24).

stenting or coronary bypass. Cardiac valve replacement had started only 3 years earlier, and repair techniques for atrio-ventricular valve regurgitation were yet to be developed. The aorta in its various segments was just beginning to be resected (by DeBakey and Cooley). Carotid endarterectomy was infrequent. Percutaneous techniques to open intracardiac obstructions or close intracardiac defects were unavailable. The Swan-Ganz catheter had not yet appeared. Pacemakers were available but they weighed 8 times what they weigh today and lasted about a fifth as long. Implantable cardioverter defibrillators were unavailable and, indeed, external cardiac defibrillation had just begun (1960). Electrophysiologic techniques to determine sites of ventricular arrhythmias and catheter and operative ablation procedures were 20 years away. Heart transplantation was 5 years away.

And drugs for cardiovascular conditions were just beginning. The first antihypertensive drug had arrived just 10 years earlier. A beta-blocker had just arrived on the scene. There were no calcium-channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, thienopyridines, glycoprotein IIb/IIIa inhibitors, or direct thrombin inhibitors. Aspirin had not yet been recognized as a cardiac disease preventive. Statins and ezetimibe were not yet discovered, and niacin had not yet been recognized as a lipid-altering agent. Digoxin, quinidine, and procaine amide were the mainstays of antiarrhythmic therapy. Lidocaine had just arrived.

Thrombolytic therapy for AMI was reported initially in 1976 by Chazov in a Russian medical journal, and the concept was lost until 5 years later when Peter Rentrop injected streptokinase directly into the "infarct-related" coronary artery in patients with AMI. He took patients with AMI directly to the cardiac catheterization laboratory, and in some patients he injected streptokinase directly into the totally occluded coronary artery and in some others he injected nitroglycerin. In the streptokinase group, the artery in most patients opened

up quickly, but it did not do so in the patients in whom nitroglycerin had been injected. At repeat catheterization 7 days later, however, the infarct-related coronary artery in both groups was patent. Thus, in this initial study, Rentrop and colleagues demonstrated in patients with AMI that the infarct-related coronary artery was totally occluded at the onset of the infarction, that streptokinase dissolved the thrombus superimposed on the atherosclerotic plaque rather quickly, and that spontaneous lysis of the thrombus did occur but that that occurrence was too late to limit the size of the acute myocardial infarct.

It was not long, of course, before other thrombolytic agents were demonstrated to be better than streptokinase and also that administration of the fibrinolytic agent by the intravenous route was as beneficial as by the intracoronary route. It was shown early that whatever thrombolytic agent was administered, the shorter the period from door to needle or from emergency medical services to needle, the better the outcome, and ideally the time should be <30 minutes. Of course, some patients have contraindications to fibrinolysis (e.g., severe hypertension; possible aortic dissection; recent trauma, surgery, or bleed; a bleeding or clotting disorder; another life-threatening condition), and therefore their only hope of salvaging myocardium is percutaneous coronary intervention (PCI).

Although coronary angioplasty had been introduced in 1978, it took some time and major persistence by several investigators to convince the cardiovascular community that primary PCI provided better hospital and 1-year outcomes than did intravenous thrombolysis as long as the time from medical contact to balloon or from door to balloon was <90 minutes—and ideally, of course, the shorter the better. An invasive strategy is now the preferred therapy, assuming both skilled personnel and equipment are available, with medical contact to balloon or door to balloon time <90 minutes.

Why has primary PCI proved to be better than thrombolysis? Some morphologic studies in the 1980s showed that the quantity of underlying plaque at the site of thrombus in patients with AMI varies from about 30% to 95% of the cross-sectional area (average, 80%) and, therefore, that the area occupied by thrombus ranges from 70% to only 5% (average, 20%) (26). Thus, thrombolytic therapy on average, when successful, opens up the artery only 20% in cross-sectional area whereas PCI, ideally including initial evacuation of the thrombus, cracks the underlying plaque and, therefore, provides a much greater opening than thrombolysis alone (27). Indeed, PCI opens the artery to a greater degree than it was before the AMI!

When I interned at Boston City Hospital in 1958, the hospital mortality in patients with AMI was about 35%. Today, without reperfusion—either by thrombolysis or PCI—that mortality is 25%. With successful thrombolysis alone it is about 7%, and with PCI alone, about 5% and even less when the thrombus is initially evacuated.

These results are remarkable! Patients with ventricular fibrillation before hospitalization and cardiogenic shock on admission continue to have very high hospital mortality rates,

as do patients with right ventricular infarction, ventricular rupture, and important mitral regurgitation. Better secondary prevention will continue to reduce the frequency of another atherosclerotic event, and better primary prevention would prevent many AMIs from ever occurring.

## PRESENT-DAY CHALLENGES OF SUCCESSFULLY MANAGING A NONSOCIETY-OWNED CARDIOVASCULAR JOURNAL

There are two basic types of medical journals: those owned by a society and those owned by a publisher. Subscription to society publications is usually included in the society's dues. Subscriptions to publisher-owned journals are paid by the subscriber directly to the publisher. Several current publisher-owned journals initially were the official journals of a society, but later the society broke the relationship. Both the *American Heart Journal* (begun in 1925) and *The American Journal of Cardiology* (AJC) (begun in 1958), for example, began as the official publications of their societies, but the journal titles were owned by the publisher. Later, the society and publisher relation dissolved but each journal continued independent of the society. *Circulation* and the *Journal of the American College of Cardiology* were the first journals owned by the American Heart Association (AHA) and the American College of Cardiology (ACC), respectively, and the publishers of their journals are under contract with the societies.

The publisher-owned journals also are of two types: 1) those with *uncontrolled* circulations, in which subscribers pay publishers directly for their subscriptions; and 2) those with *controlled* circulations, in which publishers send the journal free of charge to recipients of their choice (28). These latter journals are entirely dependent on advertisers for support. *Clinical Cardiology* is an example of a controlled-circulation journal, but it has peer-review of its manuscripts. Most purely advertiser-dependent journals—referred to as “throwaway” journals—however, are not peer-reviewed. Most publisher-owned journals—whether with uncontrolled or controlled circulations—are entirely clinically oriented. Virtually all of the basic-science cardiovascular journals are society owned.

A major challenge today for all clinical cardiovascular journals—and even more so for general medical and multispecialty journals—is the *decreasing advertising revenue for the medical journals*. The shift by pharmaceutical companies of sizeable portions of their advertising budgets directly to consumers via television, radio, newspapers, and magazines and the slowing of growth rates for the pharmaceutical companies diminish advertising monies available for medical journals. As the number of ads in medical journals decreases, subscription costs increase, which, in turn, causes the number of subscribers to decrease. As a consequence, subscriptions to nonsociety-owned medical journals have either leveled off or are decreasing. In contrast, because the number of cardiologists increases each year over the number retiring or dying, the number of subscribers to society-owned journals continues to increase. Thus, the reduction in advertising revenue potentially hurts the publisher-owned cardiovascular journals more than the society-owned cardiovascular journals. The publisher-owned journals also do not have the leverage of

some society-owned journals, which can promise prime exhibition space at their annual scientific sessions to pharmaceutical and device companies, for example, if a certain number of ads is placed in the journal in a particular year.

In 2008, eight *new US cardiovascular journals* appeared—all in a single year and all society-owned! All presently are bimonthly. The long-term effect on publisher-owned cardiovascular journals is so far unclear, but certainly this enormous influx of society-owned journals in a single year cannot be beneficial to the publisher-owned journals. The number of manuscripts submitted to the AJC in 2008 is running only slightly less than in 2007 (about 3000), but the percentage of total manuscripts submitted from non-USA countries has increased.

The more recently certified US cardiologists, nearly all of whom become members of the AHA and ACC, are accustomed to *getting their medical journals free*, which is not the case after fellowship, and having to pay for the nonsociety journals is a habit not acquired by many of the younger cardiologists. Furthermore, many of the younger cardiologists get their information online, a habit not as frequent among older cardiologists.

The *process of selecting editors-in-chief* is much different for a society-owned journal than for a publisher-owned journal. Societies have publications committees that select editors for their particular journals. The editor-in-chief of a publisher-owned cardiovascular journal serves at the pleasure of the publisher and is selected by the publisher. An independent publisher may have less access to the leaders of the cardiovascular community than do society publishing committees. (In my opinion, few society publishing committees or publishers, however, have thoughtfully developed criteria for potential editors-in-chief. Whether specified criteria would be useful in the selection process, however, is unclear.)

There is *competition among the better clinical cardiovascular journals for the better cardiovascular manuscripts*. Editors of publisher-owned journals need to be proactive in recruiting manuscripts, particularly reviews and editorials, especially from the elite among the cardiovascular community. Another means by which publisher-owned cardiovascular journals can compete effectively with society-owned cardiovascular journals is to publish manuscripts that are as clinically useful as possible, ideally applicable to the next patient seen. Manuscripts involving nonhuman animals are rarely helpful when seeing the next patient and, therefore, they were eliminated when the AJC became a publisher-run journal rather than a society-run journal. Publisher-owned journals also need features that are unique to them. The AJC, for example, publishes *interviews* of prominent cardiovascular specialists, informal *roundtables* on particular topics discussed by experts, and symposia from meetings.

Publisher-owned cardiovascular journals also must operate as efficiently as possible and deal with authors as pleasantly as possible. Manuscripts submitted to the AJC are sent out usually the following day to two potential reviewers, each of whom is asked if he or she is willing to review the particular manuscript. Most manuscript decisions are made within a month of receiving the manuscript. Revised manuscripts are usually accepted

promptly. Manuscripts declined by other journals can be submitted to the AJC along with reviews from the other journal and the author's responses to them and an "accept (with further revision)" or "reject" decision can then be made promptly.

Another way that publisher-owned cardiovascular journals can compete effectively with society-owned journals is to *publish symposia* under separate cover. These are sponsored by one or more pharmaceutical or device companies, and they are welcomed, for example, in the AJC. These are all organized by one or more guest editors. In 2008, Dr. Clyde Yancy began serving as the overall editor of all symposia submitted to the AJC. Readership surveys have shown very favorable responses to the published symposia, all of which are published under separate cover with a different color from the regular issues. No advertisements appear in the supplement issues. Symposia are profitable to the publisher and help support the regular issues.

In the past, sales of reprints have been a prominent profit source for publishers of medical journals, but now authors order far fewer reprints than they did in the past.

Like newspapers, the publishers of multiple medical journals now sell Internet packages that include access not only to a particular journal but to other journals published by the same publisher. These Internet packages are becoming important revenue sources for publishers of multiple medical journals. Electronic editions of the journal and advertisements in them, on the journal's website and in the table of contents, also are sources of revenue.

With the *open access publishing model* pioneered by BioMed Central ([www.biomedcentral.com](http://www.biomedcentral.com)) and the Public Library of Science ([www.plos.org](http://www.plos.org)), articles are made freely and permanently accessible online immediately upon publication. Bentham Open is another open-access journal devoted to various disciplines in science and technology ([www.oa.cardiovascular-med.org](http://www.oa.cardiovascular-med.org)). This type of competition almost surely will increase with time.

In summary, there are too many cardiovascular journals! Because of inadequate advertising revenue, many controlled (throwaway) publisher-owned cardiovascular journals have disappeared in recent times, and others will follow. This is not all bad. In 2008, the AHA started six new cardiovascular journals and the ACC, two new journals, all bimonthly. The long-term effect on the remaining uncontrolled publisher-owned cardiovascular journals is as yet unclear, but there will be an effect. The new journals and the enormous amount of cardiovascular information provided online, however, will surely put pressure on the publisher-owned journals to be as clinically useful as possible and to provide unique features—such as interviews, roundtables, and symposia—not available in most society-owned cardiovascular journals.



—WILLIAMS CLIFFORD ROBERTS, MD  
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