CORRESPONDENCE

The Origin of Echocardiography?

To the Editor:

I read "The origin of echocardiography: a tribute to Inge Edler" in the *Texas Heart Institute Journal*.[1] As a medical consultant to the *Journal* and as one who lived and worked during the early years of cardiac ultrasound, I feel obliged to make some corrections and additions to that article.

First of all, I was not the first person to use the term "echocardiography" to describe the ultrasonic examination of the heart. To my knowledge, the word first appeared in print in an article by Dr. Bernie Segal of Philadelphia. I avoided the use of "echocardiography" initially, because there was no abbreviation for it. The obvious abbreviation for echocardiography would be ECG, and that had been preempted by the electrocardiogram. We could not use the abbreviation "echo," because echoencephalography was still a viable entity. Only after echoencephalography ceased to exist as a diagnostic procedure were we able to adopt the term "echocardiography." That made the "echo" abbreviation available for application to echocardiography.

My collaboration with Hal Dodge had nothing to do with ultrasonic instruments. We went to Alabama, where Hal was at the time, because he was doing biplane ventriculography, which was recognized as the gold standard for determining cardiac volumes. We needed an accepted gold standard for comparison with our echocardiographic measurements.

If "father" of a technique implies that a person was the first to use or introduce it, then I am not the father of echocardiography in the United States. When I accidentally stumbled onto diagnostic ultrasound by way of an erroneous advertisement in 1963, Claude Joyner and Jack Reid had already published a paper that duplicated Dr. Edler's mitral valve diastolic E to F slope technique for evaluating mitral stenosis.[2] I was not the first in the United States to use cardiac ultrasound.

When I saw my first ultrasound instrument, it clearly could not do what was advertised—measure cardiac volume. However, when I placed the transducer on my chest and saw a moving echo from the back wall of my heart, I immediately thought that I could use the gadget to detect pericardial effusion behind the posterior left ventricular wall. It turned out that I was right, and the technique proved to be the first reliable, long-lasting diagnostic application of cardiac ultrasound,[3] with the possible exception of its use in detecting left atrial masses, which was first described by Sven Effert.[4] Although Edler showed a patient with a large pericardial effusion anterior to the heart, anterior echo-free spaces are common and are nonspecific for fluid.

My first efforts were not inspired at all by Dr. Edler or Dr. Joyner. In fact, I visited Dr. Joyner and was most unimpressed with what he was doing. I noted very early that the mitral E to F slope promoted by Dr. Edler and later by Dr. Joyner as the principal use of cardiac ultrasound was unreliable and nonspecific. I then heard Dr. Edler lecture at a general ultrasound meeting in Pittsburgh in 1965. Again, I was thoroughly unimpressed: he mentioned only the E to F slope. It became apparent that he had done no further development of the technique since his movie had been shown at the European Congress of Cardiology in 1960 and a review article had appeared in the *Acta Medica Scandinavica Supplement* in 1961.[5] I invited Dr. Edler to participate in the first meeting dedicated to cardiovascular ultrasound in January 1968 in Indianapolis. He did not lecture and only showed the 1960 movie.

The implication of the *Texas Heart Institute Journal* article is that today's practice of echocardiography is a direct result of Dr. Edler's work. That is not entirely correct. Inge worked in the field for less than 10 years. His efforts culminated in and apparently ended with the above-mentioned movie and review. Although Inge described several parts of the heart and some abnormalities that could be seen ultrasonically, the only application that he thought useful was the mitral E to F slope for the evaluation of mitral stenosis. The fact is that by the early and mid-1960s, the E to F slope already had been discredited; that disrepute cast doubt on all ultrasonic techniques, including those that were coming out of Indianapolis.

The notion that today's echocardiography is a direct result of Dr. Edler's efforts is, in today's terminology, a "disconnect." In the early and mid-1960s, cardiac ultrasound was essentially dead. At that time, I could not find anyone in the United States or Europe working in the field, other than Dr. Joyner. Hellmuth Hertz had long since left the field, and, according to Dr. Effert (who also left the field), Hellmuth advised Siemens Corporation, the company that had provided the ultrasonoscope for Edler, not to enter the field because it had no future. I suspect that when Drs. Cournand and White rejected what he was doing, Inge also gave up on cardiac ultrasound. When I visited him in Lund in 1969, he was using the technique only for the mitral E to F slope. He had not adopted any of the applications demonstrated at the meeting in Indianapolis. I was also disappointed to learn that no one in Lund or anywhere else was carrying on in the field.

Thus, in our early years, we not only had to start from scratch, but we had to overcome some serious skepticism as a consequence both of failed techniques, such as ballistocardiography, and of discredited ultrasonic applications, such as the mitral E to F slope. It was very difficult to get our papers published and to have our techniques used clinically. As a result, we had to train a whole new generation of physicians not just in the United States, but all over the world—including Europe. We did this by developing new applications, training fellows, offering multiple meetings and preceptorships, giving many lectures all over the world, and publishing numerous articles and books. It truly would have been much easier for us if we really had been the first to use cardiac ultrasound.

My wife and I had the privilege to be with Inge and his wife Karin on many occasions. They were a delightful couple. Inge was a quiet, humble, and honest man. He would have been the first to admit that if we in Indianapolis had not resurrected echocardiography from the dead in the early and mid-1960s, his work would never have been recognized.

Harvey Feigenbaum, MD,
Distinguished Professor of Medicine,
Krannert Institute of Cardiology,
Indiana University School of Medicine,
Indianapolis, Indiana

References

1. Singh S, Goyal A. The origin of echocardiography: a tribute to Inge Edler. Tex Heart Inst J 2007;34(4):431-8.
2. Joyner CR Jr, Reid JM, Bond JP. Reflected ultrasound in the assessment of mitral valve disease. Circulation 1963;27(4 Pt 1):503-11.
3. Feigenbaum H, Waldhausen JA, Hyde LP. Ultrasound diagnosis of pericardial effusion. JAMA 1965;191:711-4.
4. Effert S, Domanig E. Diagnosis of intra-auricular tumors & large thrombi with the aid of ultrasonic echography [in German]. Dtsch Med Wochenschr 1959;84(1):6-8.
5. Edler I, Gustafson A, Karlefors T, Christensson B. Ultrasound cardiography. Acta Med Scand Suppl 1961;370:5-123.

This letter was referred to Drs. Singh and Goyal, who reply in this manner:

We wish to thank Dr. Feigenbaum for his critical input and we welcome his additions, particularly in regard to the origin of the word echocardiography. His knowledge of the history of echocardiography is doubtless greater than ours, because he was so directly involved in creating that history. At the same time, we wish to reiterate our belief in the pioneering role that Dr. Edler played. In light of the extensive literature review that we performed in preparation for writing, we wish to comment on some of Dr. Feigenbaum's corrections.

Dr. Feigenbaum talks about our referring to him as the father of echocardiography in the United States, on the basis of his having introduced echocardiography there. However, we never suggested that. In fact, our article says, "It was not until a decade after Edler and Hertz's discovery of 'cardiac ultrasound' that the 1st American article on the cardiac use of diagnostic ultrasound in mitral stenosis, a duplication of Edler's work, was published by John Reid and Claude Joyner."[2]

Nor do we imply that "today's practice of echocardiography is a direct result of Dr. Edler's work." Our article's title itself professes our central intent to talk about the origin of echocardiography, rather than its evolution. We intended to convey the information that Dr. Edler originated the idea of echocardiography and that his initial work on echocardiographic technique stimulated others to work in the area. Echocardiography as it is today is the product of several investigators who worked in the field for much longer than Edler did; but the path was carved by Edler. Even Dr. Edler downplayed his own contributions, crediting those persons who were inspired by his work and continued along his path.[3]

Dr. Feigenbaum's suggestion that Dr. Edler contributed little to the development of echocardiography and, in a way, even hampered it, is unfair. The application of echocardiography to clinical evaluation in adult cardiology was a most difficult task that required anatomic and physiologic studies and, of course, an enormous number of careful, time-consuming examinations of patients. Dr. Edler did not know what exactly to look for, he had no 2-dimensional real-time image, and he was using low-sensitivity, quartz ultrasound transducers. Yet what he accomplished was an innovation with high standards of invention—a development that occurred despite his lack of suitable high-speed electronic components, sufficiently fast computers, and advanced ultrasonic transducers that could completely explore the inherent possibilities of the method.[4]

Then too, Dr. Edler was closely involved in the development of the first 2-dimensional real-time images of the heart, which were presented in 1967 at the Lund Institute of Technology.[5] Along with Nils-Rune Lundström, he also explored the use of the Doppler effect in ultrasonic measurement of intracardiac blood flow. Dr. Edler's acumen in cardiac auscultation and phonocardiography enabled him to distinguish the sound of blood flow in a very noisy signal, a signal interpreted in the past as due to the movement of heart muscle and valve leaflets. He presented the first 40 clinical Doppler recordings for evaluation of aortic and mitral valve incompetence at the first World Conference in Ultrasound Diagnosis in Vienna, in 1969.[6] He also made the first attempt at transesophageal echocardiography, a feat that was eventually accomplished more than 2 decades later.[7] Much of this work was carried out by Dr. Edler after the callous rejection of his early efforts by Drs.

White and Cournand in 1956, and after his making of the 1960 film to which Dr. Feigenbaum alludes.

While we respect Dr. Feigenbaum's additions to our article and to the field of echocardiography, we do not believe that we overstated Dr. Edler's pioneering contribution to medical diagnosis.

Siddharth Singh, MBBS, Postdoctoral Scholar,
Division of Gastroenterology/Physiology,
University of California,
Los Angeles;
and
Abha Goyal, MBBS, Postdoctoral Scholar,
Division of Hematology and Oncology,
University of California,
Los Angeles

References

1. Feigenbaum H. Evolution of echocardiography. Circulation 1996;93(7):1321-7.
2. Singh S, Goyal A. The origin of echocardiography: a tribute to Inge Edler. Tex Heart Inst J 2007;34(4):431-8.
3. Rakowski H. Lives Lived: Inge Edler [presidential address]. Raleigh, NC: American Society of Echocardiography; c2007 [2001 May; cited 2005 Jul 23]. Available from: http://www.asecho.org/Archives/Presidents_Message/body_may01.php
4. In memoriam. Inge Edler: the father of echocardiography. Eur J Echocardiogr 2001;2(1):1-2.
5. Asberg A. Ultrasonic cinematography of the living heart. Ultrasonics 1967;5:113-7.
6. Lindstrom K, Edler I. Ultrasonic Doppler technique in heart disease--I. an experimental study. II. Clinical application. In: Bock J, Ossonig K, editors. Proceedings of the First World Congress on Ultrasonic Diagnostics in Medicine. Vienna; 1969.
7. Edler I, Lindstrom K. The history of echocardiography. Ultrasound Med Biol 2004;30(12):1565-644.

Lambl's Excrescences: Is Surgical Excision Really Necessary?

To the Editor:

We read with great interest the recent article by Aziz and Baciewicz, titled "Lambl's Excrescences: Review and Recommendations."[1] In that report, the authors recommend surgical débridement as standard management for patients who have "giant" Lambl's excrescences (LE) with recurrent neurologic events.

Previous studies investigating the association of valve strands or excrescences with stroke have been limited by their inconsistent methodology, nonstandardized diagnostic approaches, and retrospective design.[2,3] Hence, the results do not allow definitive conclusions regarding the role of valve strands in causing central nervous system events.

The embolic risk of valve excrescences was evaluated prospectively in an investigation by Roldan and colleagues,[4] in which 90 healthy subjects and 88 patients with or without suspected cardioembolism were studied and followed clinically for approximately 4 years. The prevalence of valve excrescences in healthy subjects (38%) and in patients with (47%) or without (41%) suspected cardioembolism was similar irrespective of age or sex, and the presence of valve excrescences did not appear to be associated with future embolic events. These findings suggest that there may not be a direct causal link between ischemic stroke and the presence of the valve strands. Perhaps these filaments are simply "innocent bystanders" of no pathophysiologic significance. In addition, differentiating a "giant" excrescence from a "small" papillary fibroelastoma (PFE) can be challenging. It is possible that these lesions might be part of a pathologic "spectrum" with some degree of overlap, especially with the larger excrescences.

In contrast with PFE, the current medical literature does not support surgical removal of valve strands or excrescences.[5] In a patient with recurrent neurologic events that are presumed to be embolic without other explanation, in whom valve excrescences are found on transesophageal echocardiography, it is reasonable to consider anticoagulation, preferably with aspirin. In our opinion, surgical excision of these lesions should not be recommended as a standard approach, because these excrescences have not been proved to cause central nervous system events. We recognize that there may be occasional exceptions, especially when large lesions with a head or a stalk are found, but these lesions should more properly be termed PFE, instead of LE.

Rowlens M. Melduni, MD, FASE, FACC,
Kyle W. Klarich, MD, FACC,
Gillian C. Nesbitt, MD, and
Clarence Shub, MD,
Division of Cardiovascular Diseases,
Mayo Clinic,
Rochester, Minnesota

References

1. Aziz F, Baciewicz FA Jr. Lambl's excrescences: review and recommendations. Tex Heart Inst J 2007;34(3):366-8.
2. Lee RJ, Bartzokis T, Yeoh TK, Grogin HR, Choi D, Schnittger I. Enhanced detection of intracardiac sources of cerebral emboli by transesophageal echocardiography. Stroke 1991;22(6):734-9.
3. Freedberg RS, Goodkin GM, Perez JL, Tunick PA, Kronzon I. Valve strands are strongly associated with systemic embolization: a transesophageal echocardiographic study. J Am Coll Cardiol 1995;26(7):1709-12.
4. Roldan CA, Shively BK, Crawford MH. Valve excrescences: prevalence, evolution and risk for cardioembolism. J Am Coll Cardiol 1997;30(5):1308-14.
5. Klarich KW, Enriquez-Sarano M, Gura GM, Edwards WD, Tajik AJ, Seward JB. Papillary fibroelastoma: echocardiographic characteristics for diagnosis and pathologic correlation. J Am Coll Cardiol 1997;30(3):784-90.

This letter was referred to Drs. Aziz and Baciewicz, who reply in this manner:

We thank Dr. Melduni and his associates for their interest in our case report.[1] We agree that the conservative management of Lambl's excrescences (LE) should be the 1st line of treatment. We do not recommend surgical débridement as the standard management of LE. However, any cerebrovascular accident (CVA) should prompt an investigation of a possible embolic cause.

As we outlined in our manuscript, patients with LE can be divided into 3 broad categories:

- *Asymptomatic Patients with LE.* We recommend close follow-up with serial echocardiograms for this group of patients.
- *Patients Who Have LE and Have Experienced 1 CVA* (with no alternative source of emboli identified). We recommend that these patients be treated medically with anticoagulation (coumadin, or aspirin and clopidogrel).
- *Patients with LE and a History of 1 CVA Who Are Already on Systemic Anticoagulation.* If these patients experience a 2nd CVA, we recommend surgical débridement of LE.

A detailed review of the prospective study by Roldan and colleagues[2] (alluded to by Melduni and associates) shows that 37% to 40% of patients with LE remain asymptomatic—a number larger than expected. However, the mean follow-up time for this study was only 31 months. It is difficult to conclude that these patients would remain asymptomatic if they were followed for a long time. A review of the medical literature reveals no long-term follow-up of asymptomatic patients with LE.

Accordingly, we can only speculate that a very small percentage of these asymptomatic patients will become symptomatic. We recommend anticoagulation for patients who become symptomatic. Only those patients who continue to have symptoms while taking anticoagulants should be offered surgical débridement of LE. With application of these recommendations, a very small percentage of LE patients will be offered an operation.

Faisal Aziz, MD,
Department of Surgery,
New York Medical College,
Valhalla, New York;
and
Frank A. Baciewicz, Jr., MD,
Section of Cardiothoracic Surgery,
Wayne State University, and
Harper University Hospital;
Detroit, Michigan

References

1. Aziz F, Baciewicz FA Jr. Lambl's excrescences: review and recommendations. Tex Heart Inst J 2007;34(3):366-8.
2. Roldan CA, Shively BK, Crawford MH. Valve excrescences: prevalence, evolution and risk for cardioembolism. J Am Coll Cardiol 1997;30(5):1308-14.

On the Death of Arthur Keats

To the Editor:

Only recently did I learn from a neighbor that Arthur Keats had died. She made it clear that he'd meant for his passing to go unnoticed, without the usual institutional dirges rolling over his memory. He was a good guy, and we remember him with affection.

My wife, Debbie, worked with Dr. Keats in Cardiac Recovery at St. Luke's in the '80s. When the beds began to back up with too many postoperative cardiac patients, Dr. Keats and Debbie would go through the unit, deciding who could go up to make room for the day's surgery, and who would get to stay. They had a good relationship. When an overzealous nurse caught his attention, he'd put the situation right: "Debbie, your nurses are playing doctor again."

Dr. Keats was a superb clinician who believed in his own clinical judgment and substituted good care for a multitude of lines and drugs. Because he saw little benefit in invasive hemodynamic monitoring, pulmonary capillary wedge pressures held no interest for him. Once in a great while, he might have floated a Swan or a central venous line, but he relied mainly on his own knowledge of the patient's status. And it worked.

When I came to Houston from Virginia to head up the operating rooms at St. Luke's, Texas Children's Hospital, and the Texas Heart Institute, I was astonished to find that chest drains for postop pumps emptied into simple glass bottles: the rattle of disposable Pleur-evacs® was unknown here. In the operating rooms at the University of Virginia, I'd grown accustomed to working with Dr. Cooley's fellow resident, W.H. Muller. Dr. Muller's nurses kept 3 back tables of instruments and drugs and as many Mayo stands. By contrast, in Cooley's surgery, there was a single back table (with a couple of strings of instruments) and a single Mayo. Both Arthur Keats and Denton Cooley held to the doctrine of "less is more."

Dr. Keats was good to work with. We'd often get together in his office for a cigarette and catch up on what mattered. When the usual organizational practices (not to be confused with clinical practice) became too much fun, Dr. Keats was a good reference point for sanity.

Once, an ambitious administrative wonk wanted to "help" Dr. Keats by sharing the load, and when the dis-

tinguished candidate came for his interview, his time with Arthur Keats became legend: he was seated on a stool in front of Dr. Keats's desk, and it ended there.

Debbie's best memory of Dr. Keats is this: "There are some problems that don't have solutions." He was right, it was so, and ever shall be so. One of the fringe benefits of my job at St. Luke's was the authority to give VIPs stage names, in order to protect their privacy. Dr. Keats was, and remains, Rex Arthurius. We shall not see his like again.

Lawrence Noriega, PhD,
Principal, Spinnaker Health Partners,
Houston, Texas

History of Streptokinase Use in Acute Myocardial Infarction

To the Editor:

I read with great interest the excellent historical perspectives paper, "A History of Streptokinase Use in Acute Myocardial Infarction," by Messrs. Sikri and Bardia.[1] I would like to add some observations concerning Heberkinasa (recombinant streptokinase), which in my opinion has a prominent place in this wonderful history.

Heberkinasa, the only streptokinase obtained through recombinant DNA techniques, is produced by the Cuban Center of Genetic Engineering and Biotechnology. The quality control system of this center has been favorably evaluated by the World Health Organization and other international regulatory organizations.

The application of Heberkinasa in the treatment of acute myocardial infarction (AMI) began 15 years ago in Cuba. Following are some details that confirm the clinical effectiveness of this thrombolytic agent.

A clinical study involving 224 Cuban patients who had been diagnosed with AMI was performed. A randomized group was treated with 1.5×10^6 IU of intravenous Heberkinasa; the remaining patients were treated with natural streptokinase (streptase). Similar results were observed with respect to coronary patency, changes in hemostasis, and safety.[2]

From November 1992 through May 1995, a nationwide study of 2,923 AMI patients in 52 Cuban hospitals was performed to evaluate the clinical use of Heberkinasa. The study results were compared with those of an earlier survey of patients who had been treated with other substances, before Heberkinasa was introduced. Heberkinasa treatment reduced death by 28.3% (relative decrease) and 4% (absolute decrease), which amounts to 179 additional lives saved annually. Intracranial hemorrhage was reported in only 9 patients (0.3%).[3]

Further clinical use of Heberkinasa in Cuba has been monitored by means of a pharmacovigilance system. Over 7 years, a safety profile similar to those in clinical trials was observed.[4]

In 1998, the Cuban National Integrated Medical Emergency System began an active out-of-hospital thrombolysis program, wherein persons who exhibit clinical and echocardiographic characteristics of AMI are emergently administered Heberkinasa before hospital evaluation.[5] In Cuba, approximately 15,000 patients with AMI are admitted to hospitals annually. Thirty-five percent of these patients receive thrombolytic treatment with Heberkinasa. The mortality rate in this group of patients is less than 10%. As a result of the application of thrombolytic treatment with Heberkinasa, total deaths from AMI are half of what they were without such treatment.

Since its approval by our regulatory authorities, Heberkinasa has been the only thrombolytic agent used to treat AMI and other thrombotic disorders in Cuba.

Fidel M. Cáceres-Lóriga, MD, PhD,
Professor of Cardiology, Head of Teaching Department,
Institute for Cardiology and Cardiovascular Surgery,
Vedado, Havana, Cuba

References

1. Sikri N, Bardia A. A history of streptokinase use in acute myocardial infarction. Tex Heart Inst J 2007;34(3):318-27.
2. Multicenter, randomized, comparative study of recombinant vs. natural streptokinases in acute myocardial infarct (TERIMA). The TERIMA group investigators. Thrombolysis with Recombinant Streptokinase in Acute Myocardial Infarct. Thromb Haemost 1999;82(6):1605-9.
3. TERIMA Group of Investigators. TERIMA-2: national extension of thrombolytic treatment with recombinant streptokinase in acute myocardial infarct in Cuba. Thromb Haemost 2000;84(6):949-54.
4. Betancourt BY, Marrero-Miragaya MA, Jimenez-Lopez G, Valenzuela-Silva C, Garcia-Iglesias E, Hernandez-Bernal F, et al. Pharmacovigilance program to monitor adverse reactions of recombinant streptokinase in acute myocardial infarction. BMC Clin Pharmacol 2005;5:5.
5. Baiez AA, Sadosty AT. Prehospital cardiac care Cuban style. Emerg Med Serv 2004;33(9):79-80.

Erratum

In their case report "Right ventricular thrombus with Behçet's syndrome: Successful treatment with warfarin and immunosuppressive agents" (Tex Heart Inst J 2007;34(3):360-2), Sait M. Dogan and colleagues erroneously reported that they had checked antiendothelial cell antibodies and von Willebrand factor in their patient. There is no need to perform these tests in a patient with Behçet's disease, even in the presence of ventricular thrombus. The tests were in fact performed in another of the authors' patients, one who did not have Behçet's. The authors regret the error.