The recently developed Carcinoid Heart Disease Clinic at Mayo Clinic in Rochester, Minnesota, comprises cardiologists collaborating with experts from oncology, anesthesiology, and cardiac surgery to determine optimal medical, surgical, and interventional treatment options for affected patients. They also see patients who have had valve replacement surgery for carcinoid heart disease to determine prosthesis function and clinical status.

For the past 3 decades, Mayo Clinic cardiovascular medical, surgical, and anesthesia specialists as well as medical and surgical oncology specialists have provided multidisciplinary care for patients with carcinoid heart disease. During this time, more than 200 patients have had valve replacement surgery for carcinoid heart disease at Mayo Clinic. Mayo Clinic investigators have demonstrated improved survival for patients with carcinoid disease over the years compared with historical controls, in part related to valve replacement surgery.

Carcinoid heart disease affects more than 50% of patients with carcinoid tumors, derived from mid-gut neuroendocrine tissue. These tumors and their metastases produce active substances, including serotonin. Serotonin released from both the primary tumor and metastases causes thickening and dysfunction of the right-sided cardiac valves, with subsequent valve regurgitation. Patients with severe carcinoid heart disease may be asymptomatic or may present with symptoms of fatigue, dyspnea, edema, or ascites. “In patients with metastatic carcinoid disease, cardiac involvement results in reduced survival compared with those without cardiac involvement,” according to Heidi M. Connolly, MD, a cardiologist at Mayo Clinic in Rochester and director of the Carcinoid Heart Disease Clinic. “Valve replacement surgery improves the survival and symptoms of patients with carcinoid heart disease.”

Carcinoid heart disease (Figure 1) always involves the tricuspid valve, and pulmonary valve disease affects more than 60% of patients. Left-
sided valve disease occurs in 10% of patients and is thought to occur primarily in those who have an intracardiac shunt, which allows serotonin-rich blood to bypass the filter of the lungs and enter the left heart chambers. Left-sided valve disease also occurs in patients with very active metastatic disease and high circulating serotonin levels. Cardiac metastases are uncommon, occurring in 5% of patients with cardiac involvement. Endocardial right heart plaque deposition is often identified at the time of surgical inspection but rarely causes clinical right ventricular compromise.

Occasionally, identification of carcinoid heart disease is the first clue to recognizing metastatic carcinoid disease. However, in most patients, cardiac involvement occurs years after metastatic carcinoid disease is identified. An elevation in the brain natriuretic peptide level may raise clinical suspicion of carcinoid heart disease in asymptomatic patients, and some have suggested that this test be used as a screening tool. However, if clinical suspicion is high, echocardiography is the diagnostic test of choice; the echocardiographic appearance of the valves is pathognomonic (Figure 2), and valvular dysfunction can be quantified. Cardiac magnetic resonance imaging or computed tomography may provide additional important clinical information in select patients, such as assessment of right heart size and function to determine timing of operation.

There are limited medical treatment options for patients with symptomatic carcinoid heart disease. Diuretics may improve edema and ascites but generally do not relieve symptoms of dyspnea and fatigue. Patients with carcinoid heart disease are candidates for valve replacement if they have symptoms related to their valve disease and progressive right heart enlargement or dysfunction.

“Occasionally, asymptomatic patients with carcinoid heart disease are referred for valve operation to prepare the patient for liver surgery, such as debulking or transplantation,” says Dr Connolly. “Elevated right atrial pressure related to carcinoid heart disease increases the risk of liver surgery, and these patients are best treated with valve replacement before liver resection or transplantation.” Medical management, including therapy with somatostatin analogues (eg, octreotide), must be optimized before valve surgery or other interventions in an effort to avoid a potentially life-threatening carcinoid crisis in patients with carcinoid syndrome.

Bioprosthetic valves are generally preferred because of the need for future interventions and the risk of anticoagulation in patients with mechanical valve prostheses. Patch enlargement of the pulmonary annulus is sometimes indicated at the time of pulmonary valve replacement. Postoperative treatment with warfarin anticoagulation for 6 months is recommended. Valve replacement procedures can be performed at a low risk in patients with controlled metastatic carcinoid disease. In the most recent series from Mayo Clinic (2010 through 2012), cardiac surgical mortality was less than 5%. Occasionally, percutaneous intervention is feasible in patients with carcinoid heart disease, such as device closure of patent foramen ovale and valve-in-valve procedures for patients with bioprosthesis dysfunction. The multidisciplinary Carcinoid Heart Disease Clinic provides individualized review of patients with carcinoid heart disease to determine the degree of cardiac valve involvement and the best type and timing of intervention.

### Figure 2.

Two-dimensional (left) and color-flow (right) transthoracic echocardiographic images in the parasternal inflow view demonstrate classical thickening and retraction of the tricuspid valve leaflets during systole. The right-sided image demonstrated severe tricuspid valve regurgitation. RA indicates right atrium; RV, right ventricle.
When Dr Barney Clark signed the 11-page consent form to become the world’s first recipient of a permanent total artificial heart (TAH) in 1982, he did so with the hope that, regardless of the outcome, he would be helping patients with advanced heart failure by promoting a technology that could one day save many more lives. Three decades later, more than 25,000 patients have been supported on a mechanical circulatory device, either as a bridge to transplant or as destination therapy. Mayo Clinic’s surgical director of mechanical circulatory support (MCS), Lyle D. Joyce, MD, PhD, has been a part of this revolution from the beginning, having been one of the surgeons who performed that first implant in Salt Lake City (Figure 1). The field of MCS has come a long way since Dr Clark was supported for 112 days on a biventricular pulsatile device that was powered by a controller the size of a washing machine. In the current era, smaller continuous-flow left ventricular assist devices have markedly improved quality of life for MCS patients.

Nevertheless, for approximately 5% of patients with advanced heart failure, contemporary assist devices (which support only the left ventricle) fail to address the problem of biventricular failure. For these patients, the TAH has emerged as a reliable strategy for successfully bridging patients to transplant at Mayo Clinic (Figures 2 and 3). The current device was developed in response to the size limitations posed by the original 100cc Jarvik-7 device, which was implanted in Dr Clark.
Originally dubbed the “Jarvik-7-70” for its smaller 70cc ventricle, this pump was implanted successfully for the first time by Dr Joyce in 1985 as the first long-term mechanical support device implanted in a woman.

While the pump technology remains virtually identical to the pneumatically driven Jarvik device, the external components have undergone a dramatic upgrade, with advances in computer technology permitting a much smaller controller for the device. One of the primary quality-of-life limitations of the TAH for Dr Clark involved the controller, which was approximately the size of a washing machine. Today’s controller fits in a small backpack and can be carried by the patient, permitting a full range of activities. The Freedom portable driver (SynCardia Systems Inc) received US Food and Drug Administration approval in July 2014, enabling patients to return home while waiting for a donor organ. As of September 2014, the TAH has been implanted in 12 patients at Mayo Clinic in Rochester, with half of them successfully receiving transplants and 2 patients expiring on support.

Dr Joyce’s son, David L. Joyce, MD, has recently joined the Division of Cardiovascular Surgery at Mayo Clinic in Rochester and is also a member of the MCS team. He put this accomplishment in perspective: “The fact that we currently have more than 100 patients walking around in the community on some form of mechanical support is a testimony to the teamwork and technical expertise of the cardiologists, anesthesiologists, surgeons, ventricular assist device coordinators, engineers, perfusionists, nurses, and other professionals that compose our group.”

For Dr Joyce, the success of the MCS program represents the fulfillment of an improbable dream that started over 30 years ago when he was working on some of the early prototypes in the laboratory of Michael DeBakey, MD. “When you think about the rivalry that existed in Houston during the early days of the TAH, it’s truly remarkable to have a team at Mayo Clinic that combines the unique gifts of every member of the group.”

For the Drs Joyce, the opportunity to collaborate as surgeons within the same subspecialty represents a rare occurrence, given the lengthy training period that is typical for cardiac surgeons. As Dr David Joyce says, “One of the nice things about having a father who is a leading expert in your clinical area of interest and a sister (Sheri Crow, MD, pediatrics and critical care medicine at Mayo Clinic in Rochester) who has published extensively in the field of MCS is that you can almost host your own CME event right at the dinner table.”
Mayo Clinic Celebrates 100 Years of Cardiology

An Evening Celebrating 100 Years of Innovation, Quality, and Teamwork

In September 2014, more than 400 cardiovascular disease experts gathered in Rochester, Minnesota, to commemorate the 100-year anniversary of cardiovascular services at Mayo Clinic. The gala was hosted by Win-Kuang Shen, MD, chair of the Division of Cardiovascular Diseases at Mayo Clinic in Arizona, and Charanjit S. Rihal, MD, MBA, chair of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester. Historical photographs, artifacts, and memorabilia collected over the past 100 years were on display. The keynote speaker was Valentin Fuster, MD, formerly a cardiologist at Mayo Clinic, and currently physician-in-chief of Mount Sinai Hospital and director of Mount Sinai Heart in New York City. Summarized here are highlights from his address.

First of all, thank you for inviting me to participate in this fantastic occasion in the history of the Mayo Clinic cardiovascular enterprise.

I believe that all of us agree that Mayo Clinic has been, and will continue to be, an American phenomenon, since the 1880s when Drs William and Charles Mayo joined their father’s medical practice almost simultaneously with the opening of Saint Marys Hospital. This was coincidentally a revolution in surgery, facilitated by new antiseptic techniques and the general use of anesthesia, and the decision of a local order of Franciscan sisters to open and staff a needed hospital. The Mayo brothers became not only nationally recognized surgeons, but they were astute visionaries, foreseeing future opportunities in a rural area far from the distracting demands of an urban metropolitan setting.

In a historical book soon to be published, W. Bruce Fye, MD, describes the exciting early decades of cardiology at Mayo, a practice that today across all campuses sees about a quarter million patients each year, has about 250 consultants, and trains more residents and fellows than perhaps any other cardiology program in the United States. I will try modestly to “psychoanalyze” this organization to determine how such an unprecedented phenomenon developed and continues to be highly successful after 100 years. I served this institution for about 12 years. Of my many personal experiences, 2 in particular have helped me define and understand 6 fundamental principles and attributes that I believe characterize the institution’s success.

First Defining Experience

In the early 1970s I had the unique opportunity to review the medical records of the first 500 patients with tetralogy of Fallot operated on at Mayo between 1955 and 1964. This cohort included sick children who were among the first in the world to undergo open heart surgery with the new heart-lung machine. The purpose was to assess the long-term outcomes of this early and unique group of patients. Such review opened my eyes to 3 attributes of Mayo Clinic that I believe exert an important influence on its medical staff.

An Integrated, Multidisciplinary Approach

Cardiovascular surgeon John Kirklin, MD, was the first to use the heart-lung machine for open heart surgery in very sick children with congenital heart disease. Despite the initial high mortality of these children, the tremendous courage and faith in the success of the Mayo team was obvious. Such an integrated and multidisciplinary approach to the practice of medicine is and will continue to be a fundamental Mayo principle.

Innovation Through Clinical Research and Educational Discipline

Personally, Dr Kirklin had a huge impact on me. With the death of each of those first patients, his reaction was one of the great humility, expressing his deep disappointment and commenting in detail about the final discussion with the parents of the deceased child. He was the first real scholar who taught me to write a paper 10 times until it was close to perfection. Mayo has produced an extraordinary corps of giants like Dr Kirklin in both the medical and the surgical cardiovascular fields over 100 years. Clinical research and educational discipline are long-standing characteristics of this institution, as is commitment to patient care—a unique trilogy.
Outstanding Administrative Organization
Finally, what can I say about this first experience in dealing with 500 medical records of patients operated in the 1950s? I recall that not even a single medical record was lost. In fact, a lost record at Mayo was almost unheard of during my nearly 12 years of exposure to charts, retroactive studies, and patients, a tribute to an administratively outstanding organization.

Second Defining Experience
A subsequent or second defining experience portrays 3 additional fundamental principles closer to each of us personally. This experience occurred in the mid 1970s on a frigid day in February. The day was so cold that those of us who lived in Homestead Village had difficulties starting our cars, even with all the usual precautions of circulating hot water around the engine at night. I arrived late to work, as did a colleague and friend with rather long hair and a speedy car who was supposed to be in the cardiac catheterization lab at Saint Marys Hospital half an hour earlier. My friend arrived at the cath lab, running with his long hair flying and a police officer chasing after him; he had been caught speeding. Drs Barry Rutherford and Robert Frye calmly met them at the door.

The Power of Resilience
Rochester winters may be a contributor to the development of stoic, strong physicians, even the power of resilience, defined as the “ability to bounce back from adversity and successfully adapt to the demands of difficult situations.” I feel the great power and virtue of resilience is part of this environment.

Mutual Respect
What happened to my speedy friend, Barry Rutherford and Bob Frye, and the police officer? The police officer disappeared, but my friend was anxiously expecting an explosion from Drs Rutherford and Frye. Dr Rutherford returned to the cath lab, asking for the “next patient on the table.” I do not know details about the subsequent interaction between Bob Frye and my friend. The point is that the next day all 3 of them were at work as though nothing had happened. What distinguishes Mayo Clinic from many other institutions is mutual respect and generosity, a culture of respect and tolerance from the seniors toward the juniors and respect and trust from the juniors toward the seniors.

A Stable Support System
This example of a freezing day with intrusion of the police at Saint Marys Hospital reveals a third and very important characteristic, a personal and stable support system. If an episode like the one related had taken place in any of the 3 other institutions at which I have served, my friend’s survival on the staff would have been close to zero. For the record, my friend is today one of the leading cardiologists in Latin America.

Historical Context for Defining Experiences
In the last part of this presentation, I will unravel some of the greatest historical accomplishments of the Mayo cardiology enterprise, demonstrating that each success was based by at least 1 of the 6 fundamental principles that I described in the 2 personal experiences.

An Integrated, Multidisciplinary Approach
Seven men from the Mayo Clinic staff met with Dr Kirklin at his home on October 21, 1952: cardiologist Howard Burchell, physiologists Earl Wood and Jeremy Swan, biomedical engineer Richard Jones, experimental surgeons David Donald and John Grindlay, and cardiac pathologist Jesse Ed-
wards. Their purpose was to develop a Mayo version of the Gibbon heart-lung machine for use during open heart surgery, culminating in the first successful open heart surgery to correct a ventricular septal defect (VSD) on March 22, 1955. Journalists from around the world jumped to credit Dr Kirklin or Dr Wood, but the Mayo spokesman corrected them, saying that, as in all research projects at Mayo, this work represented the contribution of a number of investigators.

An integrated and multidisciplinary approach, although challenged today by a number of socioeconomic forces, remains and distinguishes Mayo from most other academic institutions.

**Innovation Through Clinical Research and Educational Discipline**

The electrocardiogram, invented in the Netherlands in 1902, stimulated the development of cardiology as a specialty around World War I. Mayo Clinic acquired this technology in 1914 and was one of the first institutions to apply it clinically, thanks to fellow Fredrick Willius, MD, who became Mayo’s first cardiologist and is considered by some to be the father of the specialty in this country. Not yet mentioned are the large number of cardiovascular educators—investigators that Mayo has produced and continues to produce—individuals such as Dwight McGoon, Gordon Danielson, Francisco Puga, Hartzell Schaff, A. Jamil Tajik, James Seward, John Shepherd, Geoff Hartzler, Ben McCallister, Barry Rutherford, Shahbudin Rahimtoola, and Robert Frye, and many others. In my view, education and clinical research at Mayo are and have been highly developed and nurtured, as much as the main mission of the institution: patient care.

**Outstanding Administrative Organization**

The medical records system, the electronic medical record, cardiovascular technologies, and the rapid expansion of the Mayo Clinic Health System—these are all tightly developed processes, administratively sustained over the years. Many team-oriented cardiovascular specialists in other academic institutions would like to emulate these processes.

**The Power of Resilience**

Perhaps as a result of the weather, resilience is part of the Minnesota personality. The Great Depression in the early 1930s forced Mayo to cut salaries and reduce expenses; nevertheless, it was during this difficult period that the institution created the first staffed vascular and hypertension section in the United States. And it was during World War II that physiologist Earl Wood not only developed a critical research program that focused on ways to protect fighter pilots from blackouts due to high gravitational forces, but additionally he created a premier cardiac catheterization laboratory. Also, for the record, the famous Mayo dye curves to assess cardiac shunts evolved because of the financial difficulties then encountered in the acquisition of angiographic technology.

**Mutual Respect**

Within a very competitive environment, when Mayo Clinic and the University of Minnesota were both striving to be the first to perform a successful open heart operation, C. Walton Lillehei, MD, a cardiovascular surgeon at the University of Minnesota, drove to Rochester in March 1954. He was planning to use a cross-circulation technique on a very sick child with a VSD, and he wanted to visit cardiac pathologist Jesse Edwards to study Mayo’s large collection of congenitally deformed hearts. Without hesitation and with respect and generosity, Dr Edwards showed Dr Lillehei 50 hearts with VSDs to help him plan for the operation. Respect and generosity toward the patients, staff, and visitors are daily experiences that distinguish Mayo Clinic from others.

**A Stable Support System**

Finally, perhaps this is the time to mention the extraordinary personal and stable support system that all of us experienced at the most vulnerable stage of our careers, when we were young trainees. This is easily illustrated by 2 individuals as representative providers of such important values, Dwight McGoon and Robert Frye. Their humble and stable personalities, interest in others, and passion to help in the most difficult times that we all had make them, in my view, clear examples of what this institution has meant and will continue to mean to all of us.

**Conclusion**

Mayo Clinic has been and will continue to be an American phenomenon. And the cardiovascular enterprise is and has been a most important part of this unprecedented reality.
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