A History of Innovation
CARDIAC SURGERY IN MINNESOTA

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For centuries, the heart was believed to be an inoperable organ. Through the development of new technologies and techniques, the initial difficulties inherent with operating on a moving organ began to fade. But as surgeons in the last century pushed the boundaries of cardiac repair, new problems arose. To solve them, they enlisted the help of physiologists, residents and engineers. By taking a multidisciplinary approach, sharing information and ideas, and working collaboratively, University of Minnesota and Mayo Clinic investigators found themselves at the forefront of cardiac surgery. This article reviews Minnesota’s contributions to the field.

“There, for a shining moment, the only institutions where one could go for open heart surgery were 90 miles apart, at the Mayo Clinic and the University of Minnesota.”

— Norman Shumway, MD

In the mid-1900s, the University of Minnesota and Mayo Clinic were at the forefront of cardiac surgery. Researchers from these two institutions developed techniques and devices that made heart surgery possible and spawned a medical device industry. The achievements of key individuals have long been recognized. This article suggests Minnesota’s contributions to cardiac surgery were not only the result of efforts by individuals but also by teams of surgeons and surgical residents, physiologists and engineers working together.

THE EARLY YEARS

As surgery involving other organs advanced, Aristotle’s conviction that the heart was inoperable prevailed and most surgeons viewed operating on the heart as taboo. That thinking was challenged to some extent in the early 19th century with the development of extracardiac procedures for treating penetrating thoracic injuries. Although cases of survival after surgery on the pericardium were documented as early as 1801, cardiac surgery at the end of the 19th century remained very limited. Austrian surgeon Theodor Billroth, who is considered the father of modern abdominal surgery, called it “an intervention which some surgeons would term a prostitution of the surgical act and other madness.”

During the first half of the 20th century, cardiac surgery was limited primarily to the management of traumatic injuries. Dwight Harken, MD, a World War II combat surgeon, discovered it was possible to make a small incision in a beating heart and insert a finger to locate and remove a bullet or fragment of shrapnel. The early successes of Harken and other combat surgeons as well as the development of extracardiac procedures such as closure of the patent ductus arteriosus in 1939, repair of an aortic coarctation in 1945 and development of the Blalock-Taussig shunt for treating cyanotic heart disease in the 1940s convinced surgeons that they could at least operate near the heart. Subsequently, they devised methods for repairing simple atrial septal defects (ASDs). One involved closing the defect beneath a pool of blood. However, because results were imprecise and repair of more complex intracardiac defects required direct visualization, they needed to find a way to stop blood flowing through the heart long enough to correct the problem while avoiding exsanguination.

THE BIRTH OF CARDIOPULMONARY BYPASS

In 1945, University of Minnesota chief of surgery Owen Wangensteen, MD, PhD, recognized this problem and suggested that surgical staff member Clarence Den-
niss, MD, PhD, consider developing a pump and oxygenator circuit that would support the body during cardiovascular surgical procedures. In 1947, Dennis, along with fellow surgeon Richard Varco, MD, PhD, began working on a machine to facilitate cardiopulmonary bypass. The team developed a cardiopulmonary support system that employed a series of discs rotating in an extracorporeal pool of venous blood to expose it to oxygen so gaseous exchange would take place. Their development was a massively complex machine that required 16 people to operate. The first clinical trials of the device were conducted in 1951. Unfortunately, because of inaccurate preoperative diagnoses and technician error, the first two patients to undergo surgery with the cardiopulmonary support system died. The system, however, was considered successful, as it proved that a patient's heart and lung function could be maintained during intracardiac surgery using mechanical support.

Their experience with the device made researchers realize they needed to simplify the technology in order to minimize the chance of operator error. Dennis and Varco's efforts to develop an oxygenator system were not the first. John Gibbon, MD, a surgeon at Jefferson Medical College in Philadelphia, had been working on a screen oxygenator system since 1937. He attempted to close a presumed ASD in a 1-year-old child using the cardiopulmonary bypass machine in 1952. Unfortunately, the preoperative diagnosis was incorrect (the patient in fact had a patent ductus arteriosus) and the patient died during the operation. Gibbon persevered and in 1953 successfully closed an ASD in an 18-year-old woman using his screen oxygenator device. Although this operation was successful, it was followed by five consecutive attempts at intracardiac repair that resulted in death. Discouraged, Gibbon ceased development of cardiopulmonary bypass and attempts at intracardiac surgery.

SPECIALIZED SUPPORT SYSTEMS
While Dennis and Varco were developing their heart-lung bypass machine, William Bigelow, MD, a Canadian surgeon who trained at the University of Minnesota, was working on an alternative approach. He noticed that hibernating animals had drastically slower heart rates. He therefore began animal experiments with controlled hypothermia, demonstrating that the heart could be opened and operated on for approximately 10 minutes without permanent damage. A slowed heart rate and lowered metabolic demand provided a relatively stable platform for surgery.

In 1952, John Lewis, MD, PhD, and C. Walton Lillehei, MD, PhD, performed the first open-heart procedure using whole-body hypothermia. The patient, a 5-year-old girl born with an ASD, was cooled to 27°C (81°F) using a special blanket. As a result, her brain and other tissues required less oxygen, and her heart rate slowed enough so Lewis and Lillehei could repair the defect. Although it was considered groundbreaking, the hypothermic protocol only allowed surgeons to repair relatively simple defects that could be completed in 10 minutes or less.

To do more complex repairs, surgeons needed a more sophisticated method for maintaining physiologic homeostasis. Lillehei and Morley Cohen, MD, PhD, a surgical resident and investigator at the University of Minnesota who would eventually become an expert in the oxygenation of blood, began studying techniques that would provide surgeons with more time to perform intracardiac repairs. The first experiments used a dog’s autologous pulmonary lobe as an organic oxygenator. Although the oxygenator was functional and successful overall, it was too delicate to be used clinically and edema formed.
with higher flows or any obstruction to venous outflow.\textsuperscript{10}

Given the limitations of early attempts at mechanical support, a University of Minnesota team that included Cohen, Lillehei and Herbert Warden, a colleague of Cohen’s, came up with a simple solution: using a surrogate patient for cardiopulmonary support in a technique termed “controlled cross-circulation.”\textsuperscript{11-13} The donor’s and recipient’s blood types were matched and major veins and arteries connected, bypassing the patient’s heart. This allowed the surgical staff more time to repair complex intracardiac defects than was possible using the hypothermic approach. Following success with experimentation on dogs, Cohen, Lillehei, Varco and Warren began clinical application of cross-circulation in 1954. Between 1954 and 1955, 45 patients were operated on using this technique; 28 survived to discharge.\textsuperscript{16-18} Deaths were attributed to the difficulty of the procedures and incomplete understanding of the complex pathology rather than failure of the support method.

During this time, surgeons achieved many “firsts” in lesion repairs including closure of ventricular septal defects, repair of atrophicventricular canals and correction of Fallot’s tetralogy.\textsuperscript{2,19} In a series of groundbreaking operations, Lillehei demonstrated that intracardiac repairs were possible with this method. His team found that they were now limited by their understanding of the pathology and anatomical structure rather than technology. To further his surgical staff’s understanding, Lillehei teamed up with a pathologist from Mayo Clinic, Jesse Edwards, MD.\textsuperscript{20,21}

Concurrently, John W. Kiriklin, MD, of Mayo Clinic was assembling a team to develop a mechanical pump-oxygenator that would overcome the limitations and failures of the donor bypass process and mechanical bypass machines. He, too, assembled a multidisciplinary team that included physiologists, pathologists, cardiologists, anesthesiologists and mechanical engineers. Kiriklin’s group built on Gibbon’s screen oxygenator design. The resulting machine was a complex device with an oxygenator consisting of 14 mesh screens. It also had several safety features including occluder mechanisms to maintain flow to the oxygenator as well as sensors for the arterial filter, pH control and venous reservoir volume. The cardiopulmonary bypass system required a large volume of blood (six units), which family members would either supply or pay for.\textsuperscript{22} The device was developed and tested over two years and eventually produced as the Mayo-Gibbon heart-lung bypass machine.\textsuperscript{22}

In 1955, the Mayo group planned a series of five operations using the cardiopulmonary bypass machine. Kiriklin and colleagues performed an intracardiac procedure on a 5-year-old child with a ventricular septal defect (VSD) on March 22, 1955.\textsuperscript{23,24} This was the first successful operation using mechanical cardiopulmonary bypass since Gibbon’s procedure in 1952. That first patient returned for a visit to Mayo Clinic 50 years later. With the success of the procedure, Kiriklin’s series of five patients became a series of eight.\textsuperscript{1,25} In addition, operating the bypass machine, which originally required more than a dozen people, was simplified so it could be managed by a smaller team.
As a result of these revolutionary scientific and technical discoveries, heart surgery became routine.18

THE FIRST PACEMAKERS

Despite the success of mechanical systems for cardiopulmonary support, intracardiac repair was limited by inadequate knowledge of the cardiac conduction system and inability to correct bradyarrhythmia. When complete atrioventricular block developed, mortality was 100 percent. During a discussion of the problem of heart block at a conference, Jack Johnson, PhD, an investigator in the physiology department at the University of Minnesota, suggested using a Grass stimulator, which had been used in research on frog hearts, to temporarily pace the patient’s heart.27 The stimulator would emit a small electrical charge and stimulate muscle contractions, thereby overcoming major heart block. Soon after, Vincent Gott, MD, a surgical resident, tested the Grass stimulator on dogs. Although large and cumbersome, the device was effective. Following the canine experiments, Lillehei had a patient who developed complete heart block during an operation. He called Gott to the operating room and asked him to bring the Grass stimulator and electrodes. Together, they applied the electrodes and used electrical pacing to increase the patient’s heart rate to normal. The woman did well and was discharged on isoproterenol for heart-rate augmentation.

The problem with the electrical pacing machine was the power source. The Grass stimulator was the size of a typewriter and needed to be plugged into a standard electrical outlet. A 100-yard extension cord was needed when moving a patient from the operating room to the intensive care unit. A power outage would result in death. Lillehei enlisted Earl Bakken, an electrical engineer, to develop a portable power supply to accompany the Grass stimulator. Knowing that he needed to produce a charge that was rhythmically consistent, Bakken used the circuit diagram for a metronome to produce what would become one of the most significant medical technology breakthroughs of the 20th century. The result of his work was a small device with a power supply that could be strapped to the patient’s body. It would send properly timed charges to stimulate the heart, thus overcoming complete heart block; the device was the first portable pacemaker.27

This monumental achievement led Bakken and his brother-in-law to convert their medical equipment repair shop into a medical device company. In 1960, the company, Medtronic, developed the first implantable pacemaker, leading to the establishment of the biomedical technology industry in Minnesota.28

CONCLUSION

Breakthroughs in cardiac surgery were the result of cooperation among a number of medical and technology professionals in Minnesota. Always seeking to improve the quality of care and increase treatment options, these investigators demonstrated a commitment to incorporating creative ideas from their team members and other researchers. Their efforts led to incredible developments in medicine and spawned today’s medical technology industry. MM

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