

## Evolution of Cardiopulmonary Bypass William S. Stoney

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## Evolution of Cardiopulmonary Bypass

William S. Stoney, MD

At the end of the Second World War, the devastation of many cities in Europe, combined with the problems of reconstruction and loss of financial support, had brought European medical research to a halt. On the other hand, in the United States the war brought about an enormous amount of scientific research through the development of nuclear weapons, the mass production of penicillin, early computers, and a variety of other technological advances, some of which were eventually put to use by medical investigators.

In the immediate postwar years, Congress began 3 decades of generous funding for medical research and education through the National Institutes of Health and the Public Health Service. In the 1920s and 1930s, medical research money had been scarce, but after the war there was a flood of money. The National Institutes of Health budget for medical research in 1945 was \$180 000. By 1947, it was increased to \$4 000 000, in 1950 to \$46 000 000, and in 1974 to \$1 billion.<sup>1</sup> By 2008, the total budget just for the Heart, Lung, and Blood Institute was almost \$3 billion.

Since colonial times, it had been customary for young American physicians to spend postgraduate time in Vienna, Berlin, London, or Paris. Now the opposite was true. It became important for a young European physician to have worked for a year or so in a US medical center. The world center for medical education and research had shifted from Europe to the United States.

Postwar medical progress was also stimulated by several other programs. The Hill-Burton act of 1946 provided funds for community hospital upgrades and construction. Initially this bill provided \$75 million per year for 5 years. It was a matching plan in which local hospitals were required to raise two thirds of the new construction costs, and each hospital that received federal money was required to provide a reasonable amount of care for those who could not pay.

During this same period, the Veterans Administration adopted a policy of building new hospitals in urban settings and wherever possible developed an affiliation with the nearest medical school. This gave medical schools a major voice in selecting the medical and surgical staff. Thus, the Veterans Hospitals provided positions for medical school faculty and patients for medical student and house staff education.

Finally, in 1965 Congress passed the Medicare and Medicaid bill, which paid not only the hospital costs of the elderly

but also the fees of their physicians. Initially, the American Medical Association and many physicians opposed Medicare, but actually it brought about an additional huge infusion of money into the entire medical system. It was in this rapidly expanding and well-financed environment of the early postwar years that cardiac surgery evolved.

Cardiac surgery had begun slowly in the 1940s with just a handful of operations that could be done without the use of cardiopulmonary bypass: closure of a patent ductus,<sup>2</sup> coarctation repair,<sup>3</sup> the Blalock-Taussig shunt,<sup>4</sup> mitral commissurotomy,<sup>5</sup> and in the early 1950s closure of atrial septal defects with the use of hypothermia<sup>6</sup> or the Gross well.<sup>7</sup> However, by 1950 it became obvious to those interested in cardiac operations that a heart-lung machine would be required to deal with the majority of congenital cardiac malformations and valvular heart disease.

Such a machine would first require a safe method of anticoagulation that could be reversed at the end of the operation; second, it would require a method of pumping blood without destruction of red blood cells; and third, there would have to be a method to oxygenate blood and dissipate carbon dioxide during the time that the heart and lungs were temporarily at rest. The first 2 requirements were easily met. Heparin and protamine were readily available, and there were several pumps being used in the dairy and food industry that could be adapted. The real problem was to develop an artificial oxygenator. This turned out to be difficult.

The first attempts at cardiopulmonary bypass during those years were a series of disasters with an appalling mortality rate. Many years later, Walton Lillehei reviewed all of the open heart operations reported in the surgical literature between 1951 and 1955. During those 4 years, 18 patients were reported to have had an operation using cardiopulmonary bypass at 6 different centers. There were 17 deaths and only 1 survivor. The type of oxygenators used were film (8 patients), bubble (4 patients), monkey lung (5 patients), and autologous lung (1 patient).<sup>8</sup> Word of mouth suggested that there were a number of additional attempts that were never reported in the literature with similar results. There were stories circulated of "5 deaths in a row" and other grim rumors. Some surgeons thought that maybe the heart just would not tolerate any type of surgery no matter how it was done.

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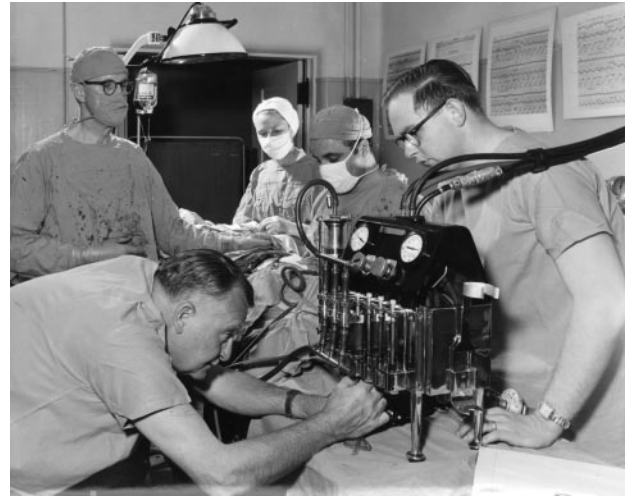
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There are several explanations for the poor early results. There was not yet a reliable cardiopulmonary apparatus available, and therefore each investigator had built his own device, sometimes based on limited laboratory experience. Another problem was the inexperience of the surgeons with this new technology. Each surgeon was self-taught, and the many small crucial details of a successful open heart operation had to be learned the hard way, by trial and error. Air embolism and postoperative bleeding were common early problems. Even the most basic steps in cannulation could be a problem because instruments, sutures, and cannulas were still evolving. Postoperative coagulopathy was almost always present. Finally, because open heart surgery was known to have such a high mortality, only the very sickest patients who were beyond medical management were referred to the surgeons. There were no institutional review boards until 1974, and therefore the decision to try a new experimental operation or device was left to the conscience of the surgeon. There was no official advocate for the patient, and informed consent was well below today's standards.

Between 1950 and 1955, 5 medical centers were actively engaged in the development of a heart-lung machine, each with a different idea of how it should function. At the University of Toronto Medical School, William Mustard developed a heart-lung machine that used isolated monkey lungs as the oxygenator. In Detroit at Wayne State Medical School, Forest Dodrill enlisted the help of engineers from General Motors to develop a heart pump, the Dodrill-GMR (General Motors Research) heart machine. It was said to look very much like an old Cadillac V-12 engine. John Gibbon at Jefferson Medical College in Philadelphia had been working on this problem longer than anyone else. His machine used DeBakey roller pumps and a film oxygenator. He had received engineering and financial assistance from the IBM Company, and his heart-lung machine was said to resemble a punch-card business machine.

At the University of Minnesota Medical School, Clarence Dennis had developed a rotating disc oxygenator based on an earlier design of Viking Björk and Clarence Crafoord. This machine used modified Dale-Shuster pumps. Also at Minnesota, C. Walton Lillehei was poised to begin a clinical trial in which the oxygenator would be either the mother or father of the patient, a technique called cross circulation. Finally, at the Mayo Clinic, John Kirklin and his colleagues were building a heart-lung machine based on the Gibbon design that used a vertical film oxygenator and roller pumps. It was called the Mayo-Gibbon heart-lung machine. In a way, it was a race to see which method would be the most successful, but at the same time it was a friendly race with continuous and generous sharing of new information and ideas at scientific meetings, visits, correspondence, and telephone calls. For example, John Kirklin described his reaction in 1954 to the news that Walt Lillehei had successfully operated on a child with a ventricular septal defect using cross circulation. "I was terribly envious and yet I was terribly admiring at the same moment and that admiration increased when a short time later a few of my colleagues and I visited Minneapolis and observed a succession of open-heart operations."<sup>9</sup>



**Figure 1.** The Dodrill-GMR heart pump. Dr Dodrill is in scrub cap and mask on the left. Used with permission from the Walter P. Reuther Library, Wayne State University, Detroit, Mich.

This is how each project evolved or was discarded. Forest D. Dodrill in Detroit enlisted the help of both the American Heart Association and the engineers from the research department of General Motors to develop a pump.<sup>10</sup> His plan (Figure 1) was to bypass only the right heart or only the left heart for less complex problems such as pulmonary stenosis or mitral valve stenosis, operations that he thought would not require an oxygenator. For more complex operations, he planned to use the patient's own lungs as the oxygenator. He reported 4 operations: 1 successful right heart bypass for a pulmonary valvotomy, 2 left heart bypass operations to explore the mitral valve with survival of both patients, and 1 total heart bypass using autologous lung as the oxygenator. This last operation involved a patient with pulmonary stenosis who did not survive. He did not pursue this technique after the first 4 operations.

Dodrill's idea of a right and left bypass circuit with the use of the patient's lungs as an oxygenator was reintroduced in 1959 by Charles Drew at Westminster Hospital in London.<sup>11</sup> Drew used a heat exchanger in the circuit to cool the patient to 15°C. The pump was then turned off, and the heart defect was repaired with the use of a period of total body circulatory arrest for as long as 60 minutes. Cardiopulmonary bypass was then resumed, and the patient was slowly rewarmed. Because of rumors of neurological injuries, this technique of profound hypothermia did not gain wide acceptance but was revived again in the 1980s and became a useful technique in a time when heart-lung machines and techniques were better understood and more reliable.

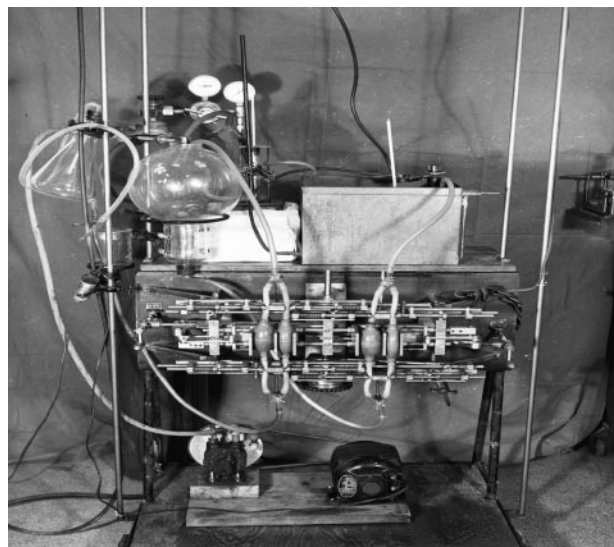
William T. Mustard was a young pediatric orthopedic surgeon in Toronto (Figure 2). Among other contributions, he had developed a muscle transfer operation to improve the walking ability of children who had poliomyelitis. He was asked by one of the senior surgeons, Albert LeMurier, to consider starting a cardiac surgery program at the Hospital for Sick Children. LeMurier was particularly interested in the Blalock-Taussig shunt for children with tetralogy of Fallot. In 1947, Mustard spent a month observing Alfred Blalock at Johns Hopkins. Returning to Toronto, he established a car-



**Figure 2.** William T. Mustard, MD. Used with permission from the Hospital Library and Archives, Hospital for Sick Children, Toronto, Ontario, Canada.

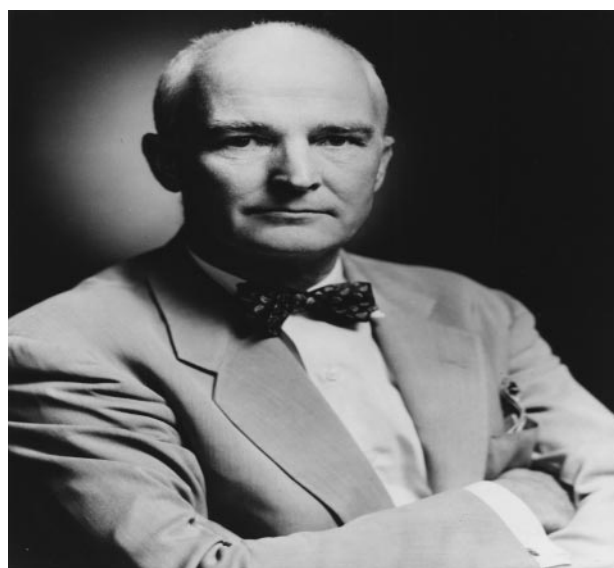
diac surgical service with operations for patent ductus arteriosus, coarctation of the aorta, and the Blalock-Taussig shunt. He developed a special skill for operating on small infants with patent ductus arteriosus and coarctation of the aorta. Like several others, he began investigating methods to move on to open heart operations. He used dogs for his experiments. His pump used 4 rubber bulbs much like the ones used on blood pressure cuffs. His laboratory oxygenator was the isolated lung of another dog. When he began operations on children, he used a pair of rhesus monkey lungs (Figure 3) as the oxygenator. At that time, rhesus monkeys could be obtained for \$40 each. Mustard's first 7 open heart operations using this method were disastrous. All 7 patients died, and the deaths were from a variety of problems.<sup>12</sup> The biggest problem was that these patients had high-risk cardiac malformations such as transposition of the great vessels or tricuspid atresia. Other contributing problems were those common to all of the first open heart operations of that time: poor myocardial protection, accidental intraoperative air embolism, erroneous preoperative diagnosis, postoperative bleeding, and a host of other similar problems. Mustard eventually reported operating on another 21 children between 1951 and 1956 using a monkey lung oxygenator, with only 3 survivors.<sup>13</sup> Dodrill's homologous lung technique and Mustard's heterologous lung oxygenator were not thought by others to be the path to success, and both methods were abandoned.

The person with the longest commitment to the development of a heart-lung machine was John Gibbon at Jefferson Medical College. John Gibbon had graduated from Jefferson



**Figure 3.** Heart-lung machine developed by C.R. Cowan and William Mustard. Rhesus monkey lungs were suspended in the glass flask and used as the oxygenator. Used with permission from the Hospital Library and Archives, Hospital for Sick Children, Toronto, Ontario, Canada.

Medical College in 1927 and after a 2-year rotating internship at the Pennsylvania Hospital had taken a position as a research assistant to Dr Edward Churchill (Figure 4) at the Massachusetts General Hospital in Boston. One of the problems they were investigating was pulmonary embolism. Dr Churchill was interested in what was then called the Trendelenburg operation. When a massive pulmonary embolus occurs, many times the patient becomes hypotensive and short of breath for as long as several hours, long enough for the cause of the problem to be recognized and theoretically long enough to perform a pulmonary artery embolectomy. In the fall of 1930, Dr Churchill was asked to see a patient who had suddenly become hypotensive and short of breath several days after having a cholecystectomy. It was thought that she



**Figure 4.** John H. Gibbon, MD. Courtesy of Thomas Jefferson University Archives and Special Collections.



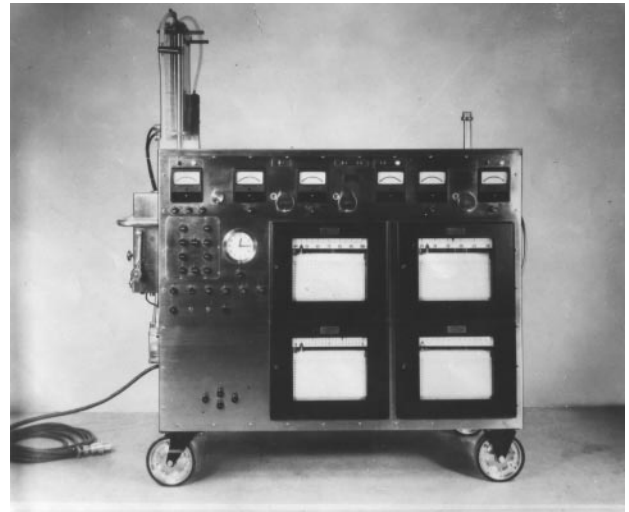
had sustained a pulmonary embolus. The plan was to attempt a pulmonary embolectomy but not until it was fairly certain that the patient was close to death. Gibbon was assigned to stay with the patient during the night to record her vital signs every 15 minutes with the plan to notify the surgical team if she appeared to be close to death. He watched that night as her venous distention and cyanosis increased and her blood pressure gradually declined. He realized that what was needed was a way to remove her venous blood, expose it to oxygen, and return it to her arterial system. Using such an apparatus, they could then restore her blood pressure and remove the pulmonary embolus.<sup>14</sup>

Early the next morning, she was taken to the operating room and the pulmonary embolus was removed, but she did not survive. In the next few weeks, Gibbon decided that the development of a pump-oxygenator for pulmonary embolectomy would be a worthwhile project. His colleagues and advisors all thought it was too difficult a problem with a low probability of success. At the end of his fellowship year, he married his laboratory assistant, Mary Hopkinson, and they returned to Philadelphia, where he continued his surgical training at the University of Pennsylvania Hospital.

His interest in the possibility of artificial circulation continued, and he asked Dr Churchill if he could return to Boston for another year in the laboratory to work on this project. Churchill agreed, and in 1934 he and his family returned to Boston. During that year he assembled a working heart-lung machine that could sustain the circulation of a cat for 30 minutes, during which time the pulmonary artery was totally occluded. He used second-hand Dale-Shuster pumps, and the oxygenator was a rotating steel cylinder. Blood was introduced at the top and flowed down as a film on the inner surface of the cylinder while being exposed to oxygen. The flow rates used were 150 to 400 mL/min. There were a great number of problems. Although heparin was available, protamine was not, so that hematomas and excess blood loss occurred. Hemolysis almost always occurred, and there were frequent episodes of equipment failure. However, he and his wife were pleased that at times they could occlude the pulmonary artery for  $\geq 30$  minutes and sustain the circulation with their apparatus.<sup>15</sup>

In 1935, they moved back to Philadelphia, and the following year he was appointed to the surgical staff at the University of Pennsylvania. He maintained a surgical practice and continued his work in the experimental laboratory. By 1937, he had several cats survive for a week or more after cardiopulmonary bypass.

All of this was interrupted by the Second World War. He entered the Army Medical Corps in 1942 and served 2 years in the Pacific theater and another 2 years at the Galesburg Military Hospital in Illinois. At the end of the war in 1945, he returned to Philadelphia and resumed his position on the surgical staff at the University of Pennsylvania Medical School as an assistant professor. The following year, he moved to Jefferson Medical College as professor of surgery and director of surgical research. Ten years later, he became the Samuel D. Gross professor and chairman of the Department of Surgery at Jefferson. Here he resumed his research. To progress from cats to dogs, he needed a larger oxygenator,



**Figure 5.** The Gibbon-IBM heart-lung machine model II. The oxygenator screens are on the top at the left. Courtesy of Thomas Jefferson University and Archives and Special Collections.

and through a stroke of good fortune he obtained the help of Thomas Watson, the president of IBM. It happened in this way. E.J. Clark was a medical student at Jefferson and had been enlisted to work in the laboratory on the heart-lung project with Gibbon's research assistant John Templeton. Clark had been a pilot during the war in the Air Transport Service. He was engaged to the daughter of the president of Lafayette College, who was a close friend of Thomas Watson. Clark rightly thought that Watson would be interested in helping with the development of heart-lung machines. Through this connection, Gibbon was invited to meet Watson, who immediately became an enthusiastic supporter.<sup>16</sup> He assigned his chief engineer, Gustav Malmros, to work on the project, and during the years 1946–1953, IBM engineers built 3 different machines all funded by IBM. The first machine used a rotating cylinder oxygenator. Models II and III each used a vertical screen oxygenator and DeBakey roller pumps. They agreed that they would share information with other institutions and that the patents would be owned by Jefferson Medical College. Model I was used only for experimental animals, model II was used in 1952 and 1953 for the first 4 patients, and model III was used after 1955.

Model II was a heavy stainless steel machine that weighed  $>2000$  pounds and was very complex. Blood was pumped by 3 DeBakey roller pumps. The oxygenator was an enclosed battery of stainless steel screens, each 40 cm tall and 25 cm wide (Figure 5). Blood flowed down each side of 6 screens while being exposed to oxygen. This provided a surface of  $\approx 8$  m<sup>2</sup> of exposed blood, far less than the  $\approx 70$  m<sup>2</sup> of alveolar surface of a normal lung but enough to provide 100% oxygen saturation at flows up to 5 L/min.

Every possible safety feature had been incorporated into the design as well as a number of automated functions. For example, the volume and the pH of blood in the reservoir were constantly monitored by electronic devices. If the reservoir volume increased, the venous pump would slow the intake of blood from the patient, and conversely, if the volume de-

creased, the venous pump would increase its flow. A backup battery-operated generator was housed in a separate steel cabinet to be used if the operating room experienced a power failure. Both cabinets were constantly flooded with nitrogen because inflammable anesthetic agents were commonly used. Altogether it was a superb device, but it was very complex, very expensive, and somewhat temperamental, and it required 2 or 3 technicians to set it up and manage it during an operation.

By 1952, after many trials in the laboratory, Gibbon was able to operate on dogs using the heart-lung machine to circulate the blood for an hour or more, do a sham operation on the right atrium, and have 9 of 10 dogs survive. In February 1952, he and his staff judged that it was time to move to clinical application.

The first patient was a 15-month-old child who was thought to have an atrial septal defect. Cardiac catheterization had been attempted but was not completed because of her small size and heart failure. The chest was opened through a right thoracotomy. After she was placed on cardiopulmonary bypass, the right atrium was opened, but no atrial defect was found. Her condition rapidly deteriorated, and she developed cardiac arrest. A postmortem examination revealed a large patent ductus arteriosus. The preoperative diagnosis was wrong.

The second patient was an 18-year-old college student with repeated episodes of right heart failure. Cardiac catheterization confirmed that she had an atrial septal defect. The operation was done on May 6, 1953. The chest was opened through a transverse incision dividing the sternum. After being placed on cardiopulmonary bypass, a large atrial defect was closed with a continuous suture. The patient was on partial bypass for 45 minutes and total bypass for 26 minutes. There was 1 major problem with the heart-lung machine during the operation. Heparinized fresh blood had been used to prime the pump oxygenator. Each 500 mL of blood had received only 10 mg of heparin. Just as Gibbon was ready to close the defect, the oxygen saturation of the blood began to rapidly fall, and clots began to form on the oxygenator screens because of inadequate heparinization. Gibbon had planned to close the defect with a pericardial patch, but because of the drop in oxygenation, it was decided to close the defect as quickly as possible with a continuous suture and to end bypass as rapidly as possible. The patient had no adverse effect from this problem and was awake within an hour after the conclusion of the operation. Gibbon's operative note states that each 500 mL of blood should have received 25 mg of heparin. That evening he made 2 telephone calls, 1 to Alfred Blalock and the second to Clarence Crafoord, telling them the good news.

Two more operations were done in 1953. Two months after the first success, Gibbon operated on a 5-year-old female patient who also had an atrial septal defect. The heart developed ventricular fibrillation shortly after the chest incision was made. She was quickly connected to the heart-lung machine and defibrillated, but each attempt at weaning the patient from the pump-oxygenator ended with dilatation of the heart and low cardiac output. Eventually she died in the operating room.

The final patient was catheterized and had several small atrial septal defects. It had not been recognized that she also had a ventricular septal defect plus a patent ductus arteriosus. When the right atrium was opened, there was a flood of bright red blood, making visualization difficult. Gibbon closed the atrial septal defects, but the patient died after the operation. So John Gibbon did 4 open heart operations using the heart-lung machine he had developed during 19 years of laboratory work. Three of the 4 patients died in the operating room, and the fourth was a success but came close to being a disaster because of premature clotting in the oxygenator. He decided to end all open heart operations for a year and use that time to obtain a trained cardiologist and a cardiac catheterization laboratory because 2 of his 4 patients had an incorrect or incomplete diagnosis. He also decided not to attempt any more heart operations himself and designated his younger colleague, John Templeton, to head the cardiac surgical service when they resumed clinical activity a year hence.

There was very little initial excitement about this successful closure of an atrial septal defect with the use of cardiopulmonary bypass. This was due in part to Gibbon's personality. He thought of himself as a scientist and a scholar and, of course, did not seek any special recognition. His 4 operations with the use of cardiopulmonary bypass were not reported until the following year and then not in a major surgical journal. In the fall of 1954, he had been invited by Clarence Dennis to give a talk at the University of Minnesota as part of a symposium on Recent Advances in Cardiovascular Physiology and Surgery. His talk included the case reports of the 4 operations and was published in *Minnesota Medicine* in 1954.<sup>17</sup>

Another factor may have been that by 1953 there had been a number of successful operations to close an atrial septal defect with hypothermia and inflow occlusion or with a Gross well. As Denton Cooley later said, "One success and three deaths did not seem to be that great." It was not until open heart surgery evolved from its uncertain beginning that Gibbon became recognized and honored as one of the major contributors to its success. On the other hand, there was a great deal of excitement and attention about cardiac surgery developing at both the University of Minnesota and the Mayo Clinic.

It all started in 1945. The chairman of the department of surgery, Owen Wangenstein, asked his younger faculty member, Clarence Dennis, to see if he could develop a heart-lung machine. Dennis eventually assembled a workable machine using modified Dale-Shuster pumps and a rotating disc oxygenator. The discs were large circular stainless steel screens that rotated slowly on a horizontal axis. Blood flowed from the center and spread as a film over the discs while being exposed to oxygen. Using this machine, he operated on 2 patients in 1951. The first patient was thought to have an atrial septal defect but turned out to have a complex atrio-ventricular canal. The attempted repair was unsuccessful, and the patient died in the operating room.<sup>18</sup> The second operation also was for an atrial septal defect and was successful, but at the end of the operation air was accidentally pumped into the patient, and this patient also died in the operating room. That



**Figure 6.** C. Walton Lillehei, MD. Used with permission from the Lillehei Heart Institute at the University of Minnesota.

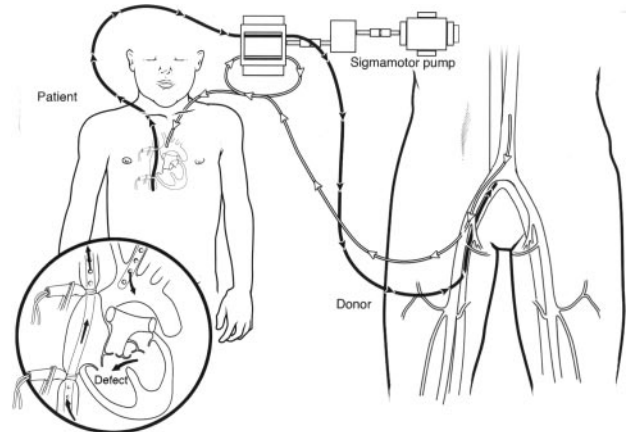
same year, Dennis moved to Brooklyn, where he accepted the position as chief of the department of surgery at Downstate Medical Center. His heart-lung machine moved there with him.

John Lewis was another member of Wangensteen's staff at Minneapolis who was investigating methods to solve the problem of open heart surgery. He had heard William Bigelow's presentation on experimental hypothermia and the possibility that a safe period of circulatory arrest could be tolerated when the body temperature was reduced. It was thought that an atrial septal defect could be closed with sutures in 5 to 7 minutes, which was the limit of safe circulatory arrest time at 30°C. A longer time would risk central nervous system ischemia. He used this technique in 1952 for a patient with an atrial septal defect named Jacqueline Johnson. After being anesthetized, she was cooled to 30°C with the use of a rubber cooling blanket that circulated cold alcohol. The vena cavae were then each clamped, the atrial septal defect was closed by a continuous suture, and the atrium was closed within the 5- to 7-minute time frame. Rewarming was managed by warm water immersion. Certainly, this had to be a nerve-wracking operation with the possibility of disaster if any delay occurred.

This operation was the first successful open heart operation ever performed.<sup>6</sup> Unfortunately, when Lewis tried to close a ventricular septal defect using this same technique, it was a failure. Hypothermia was useful only for atrial septal defects and pulmonary stenosis, both of which could be corrected in short order. Fortunately, the hypothermia technique was only used during the years 1952 to 1956 and was abandoned when safe cardiopulmonary bypass became common.

The third Wangensteen protégé of this period was C. Walton Lillehei, who is now frequently spoken of as the "father of open heart surgery." Lillehei had graduated from the University of Minnesota in 1941 and after an abbreviated internship entered the Army Medical Corps. Early in the war (Figure 6), he was sent overseas and participated in the landings in North Africa, Sicily, Salerno, and Anzio. He was a Lieutenant Colonel by the time he was discharged in 1945. He returned to Minneapolis to complete his surgical training in Wangensteen's program.

By the early 1950s, he had joined the faculty at the University of Minnesota and had participated in the advances



**Figure 7.** Diagram of the cross circulation technique used by C. Walton Lillehei in 1954–1955. Either the mother or the father of the patient was a donor.

made by Clarence Dennis and John Lewis. Two surgical residents were working with him in his experimental laboratory, Herbert Warden and Marley Cohen. They were investigating the possibility of using autologous lung as the oxygenator for cardiopulmonary bypass in dogs, a somewhat difficult technique. One evening they began discussing the function of the placenta because Cohen's wife was pregnant. During this discussion, they realized that Cohen's wife was the oxygenator for the fetus. That led them to the plan to use a large dog as the oxygenator for a much smaller dog utilizing a very low flow rate.<sup>19</sup> The low-flow perfusion technique was based on a study published by Andreasen and Watson that showed that the circulation of dogs could be temporarily reduced by 90% for up to 2 hours followed by full recovery.<sup>20</sup> The technique they used was to connect the femoral artery of the donor dog to the arterial system of the smaller recipient dog by plastic tubing. Venous blood was taken from the recipient and returned to the donor dog for oxygenation. Both circuits were controlled by a Sigmamotor pump that kept the flow rates balanced. This was called "controlled cross circulation." They were pleased to find that both donor and recipient animals recovered completely with no obvious metabolic or neurological abnormalities. After gaining confidence with this system and with the approval of Dr Wangensteen, they planned to use this technique in a clinical trial.

The first patient was a 1-year-old boy who had a ventricular septal defect. The father was the donor. The operation went well, but the patient (Figure 7) developed pneumonia and died several days later. However, the next 2 patients with ventricular septal defects did well, and a preliminary report was given at the spring meeting of the American Association for Thoracic Surgery. This technique received a great deal of attention in both the profession and in the media, some positive and some critical.<sup>21</sup> It was pointed out that the operation had obvious risks for both the recipient and the donor, and as 1 critic put it, this was "an operation that could have a 200% mortality." Lillehei went on to use this operation during the next 18 months. He was the first surgeon to successfully close a ventricular septal defect, the first to do a total repair of tetralogy of Fallot, and the first to repair a



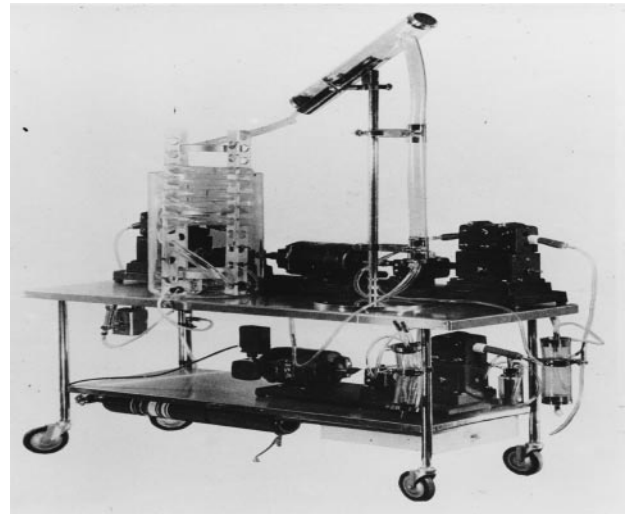
persistent common atrioventricular canal. He did 45 operations using cross circulation and had 28 survivors.

In discussions then and later, he and his associates minimized the risks to the donor, who was either the mother or father of the patient. Actually, they had 2 serious accidents involving the donor parent. An anesthesiologist accidentally pumped air into the intravenous line of a mother at the beginning of an operation. She sustained permanent cognitive loss, which eventually required long-term care.<sup>22</sup> Another mother had cardiac arrest just at the end of the cross circulation. She was resuscitated by open cardiac massage and recovered completely. Although there was great interest in this technique, it was not adopted by other surgical groups. The risk of injury of the parent acting as the donor was a major concern.

In 1954, just after the first cross circulation operation, Richard DeWall returned to the University of Minnesota from military service and was working in Lillehei's laboratory. He was appointed to oversee the setup and manage the tubing and the Sigmamotor pump during the cross circulation operations. In doing so, he became the very first open heart surgery perfusionist.

The cross circulation technique worked well enough, but it had 2 major problems. First was the obvious risk of injury to the donor, and second was the fact that it could only be used for small children. The flow rates were far too low for use in an adult. One day after an operation in which cross circulation was used, Lillehei and DeWall were talking about future operations. Lillehei pointed out that they would need an artificial oxygenator to progress to larger children and adults, and so he asked DeWall if he would like to begin working on this problem in the laboratory. Lillehei offered 2 guidelines: "First of all, do not go to bubble oxygenator systems because they have a very poor history of success. Second, avoid libraries and avoid literature searches, as I want you to keep an open mind and not be prejudiced by the mistakes of others."<sup>23</sup> He advised DeWall also to get in touch with a local company that made polyvinyl tubing for the beer and food industry, Mayon Plastics, Inc.

DeWall's first experiments involved hyperbaric saturation of the blood with O<sub>2</sub>, but this brought with it the problem of bubbles on decompression. He then began investigating using bubbles of oxygen. He set up a vertical chamber of large vinyl tubing and closed the bottom with a rubber stopper containing 18 No. 22 needles. Venous blood entered the vertical chamber at the bottom, and oxygen was connected to each of the needles. Smaller needles were found to produce foam instead of bubbles. At the top was another length of tubing, which acted as the defoaming chamber. The defoaming chamber had a gentle downward slope and was coated with a defoaming agent, Antifoam A, made by Dow Corning. DeWall noted that as the blood flowed down the slope, the lighter blood with the residual bubbles rose to the top, and the defoamed heavier blood (Figure 8) moved along the bottom of the tubing. If he used 6 feet of tubing arranged as a helix, the blood could be collected at the bottom in a reservoir, free of visible bubbles. We know now that ultrasound probably would have shown plenty of microscopic bubbles, but DeWall's system removed all of the visible bubbles. He had



**Figure 8.** An early DeWall bubble oxygenator and Sigmamotor pump. Used with permission from Richard A. DeWall, MD.

assembled a very simple heart-lung machine utilizing disposable plastic tubing and powered by a Sigmamotor model T6S pump.<sup>24</sup> After using this heart-lung machine on 10 dogs with 10 survivors, Lillehei agreed to use it in the operating room. The first use was in May 1955, and it was so successful that this inexpensive machine quickly replaced cross circulation.

The word of this new development spread rapidly through the surgical world, and Lillehei's operating room attracted visitors from all over the world. Surgeons could watch open heart operations in the morning, and in the afternoon they could visit the experimental laboratory where DeWall and Vince Gott would show them how to set up the bubble oxygenator. Before leaving, they could order a Sigmamotor pump and a collection of Mayon tubing all for <\$1000. Within a year, the Travenol Company began to market a sterile disposable copy of the DeWall oxygenator. It was this inexpensive device (Figure 9) that made it possible for many medical centers to start a cardiac surgery program. Many years later in the discussion of an article given by Lillehei, Denton Cooley stated, "Walt Lillehei brought the can opener



**Figure 9.** Richard DeWall and Vincent Gott standing beside a Travenol disposable bubble oxygenator. Used with permission from Richard A. DeWall, MD.





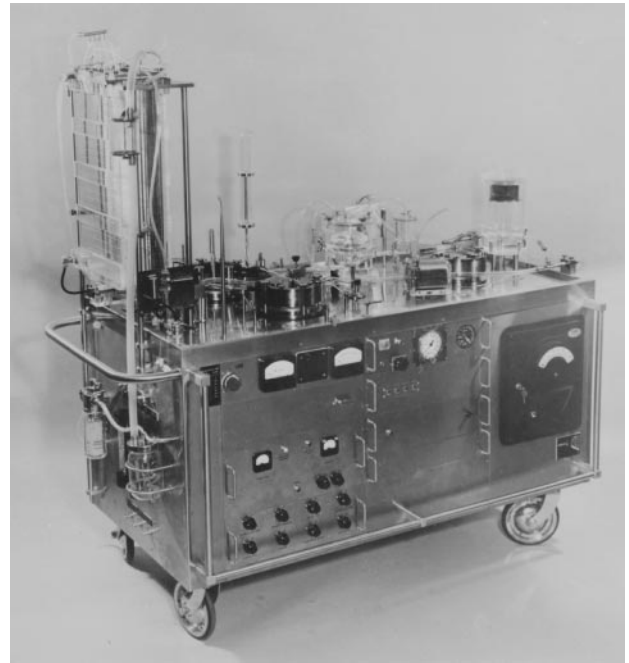
**Figure 10.** John W. Kirklin, MD. Used with permission from Lister Hill Library, University of Alabama, Birmingham.

to the cardiac surgery picnic.”<sup>25</sup> The can opener was, of course, the disposable DeWall bubble oxygenator.

C. Walton Lillehei was responsible for a whole list of innovative contributions and new ideas during the early evolution of cardiopulmonary bypass: cross circulation, the bubble oxygenator, an early cardiac pacemaker, at least 2 artificial valves, and many others. He also trained a large number of young surgeons, many of whom became chairmen of cardiac surgical programs in the United States and abroad.

Equal in stature and also from Minnesota was another giant in the specialty, John W. Kirklin. His impact on cardiac surgery brought science, discipline, and order through his own department, his leadership, and his example. As one of his colleagues said, “His lifetime ambition was to see the risk of death from cardiac surgery reduced to zero.”

Kirklin grew up in the shadow of the Mayo Clinic, where his father was the director of the Department of Radiology. His undergraduate education was at the University of Minnesota, and he graduated from Harvard Medical School first in his class in 1942. During the war (Figure 10), medical education was accelerated, so his rotating internship at the University of Pennsylvania was only 9 months, followed by 9 months of surgical residency at the Mayo Clinic. He then entered military service, and after a 6-week course in neurosurgery, he was sent to the O'Reilly General Hospital in Springfield, Mo, as a neurosurgeon. At the end of the war, he



**Figure 11.** The Mayo-Gibbon heart-lung machine. Used with permission from the Mayo Historical Unit, Mayo Clinic, Rochester, Minn.

returned to the surgical training program at the Mayo Clinic. In 1946, he spent 6 months with Robert Gross at the Boston Children's Hospital. This rotation replaced his interest in neurosurgery with a plan to concentrate on cardiac surgery. He completed his training in 1950 and became a member of the staff in the Department of Surgery at the Mayo Clinic.

In 1952, after a disappointing outcome after an operation for pulmonary stenosis, he and his colleagues, Earl Wood and David Donald, decided that a heart-lung machine was a necessity to do accurate and safe cardiac surgery. They then took a tour to visit the 3 surgeons who were involved with developing cardiopulmonary bypass: William Mustard in Toronto, Forest Dodrill in Detroit, and John Gibbon in Philadelphia. They decided to build a heart-lung machine based on the one developed by Gibbon and the IBM Company.<sup>9</sup> Gibbon very generously gave them a copy of the blueprints of his machine and the accumulated knowledge of his 17 years of laboratory work. In later years, Gibbon confessed that he was a little apprehensive that Kirklin, with all the resources of the Mayo Clinic, would be able to be the first to succeed with open heart surgery.<sup>26</sup> As it turned out, it would be 1955 before Kirklin would begin clinical trials.

The Mayo Clinic engineering department built a machine based on the Gibbon design but with some modifications. However, the basic function was the same. DeBakey pumps were used, and the oxygenator was composed of vertical stainless steel screens (Figure 11). It was very expensive to build, and it was quite complex. The only time I saw it in use was in 1958, and it required 4 technicians to get it set up and to keep it running. It was impressive and at the same time intimidating. It was called the Mayo-Gibbon heart-lung machine. They planned to begin clinical trials in March of 1955, and they scheduled 8 operations with the agreement

that they would do all 8 patients even if the first 7 died. They would then stop and review the results before proceeding to additional operations. Actually, 4 patients survived and 4 died, and from that time on they had a continuous schedule of open heart operations.

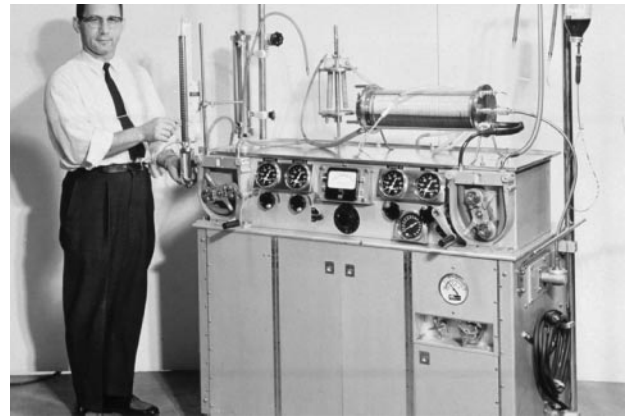
For a brief period of time (1955–1956), there were only 2 hospitals in the world where open heart surgery was being done on a daily basis: Lillehei at the University of Minnesota and, 60 miles away, John Kirklin at the Mayo Clinic. Surgeons came in droves from all over the world to see these 2 men at work. Donald Ross was one of the visitors at that time and describes his visit in this way:

When I became a consultant, Guy's Hospital sent me on a three-month sabbatical tour of America. Lillehei was still the number one man, and Kirklin was very impressive. I remember going to Minneapolis to visit Lillehei, and it was like a circus. There was a large gallery in the operating room with about fifty people. People were rushing in and rushing out. They started about seven or eight in the morning and Lillehei came in about eleven. The operating room was chaos, with pipes and tubes everywhere. The patient did very well, but I thought, I don't know if I could do this sort of surgery with so much confusion.

From Lillehei I went by bus to the Mayo Clinic to visit Kirklin. He and Lillehei were great rivals in those days. Walking into Kirklin's operating room was like walking into a church; there was no sound, no excitement. We sort of sat in pews watching him as he quietly talked. The door opened, the heart-lung machine was wheeled in and connected to the patient, and he then did the operation. I was dumbfounded that you could do this very complex procedure so quietly with no drama. Kirklin was cool and calm."<sup>27</sup>

If you wanted a heart lung machine in the early 1950s, it was necessary to build it yourself. By 1956, it was clear that Mustard's technique using monkey lungs was not realistic, and Dodrill's plan to use the patient's lung was also impractical. Three types of oxygenators had evolved by 1955: the vertical screen oxygenator of Gibbon and Kirklin, the bubble oxygenator of DeWall and Lillehei, and a rotating disc oxygenator developed by Jerome Kay and Frederick Cross in Cleveland based on the design of Björk.<sup>28</sup> By 1958 (Figure 12), each of these could be obtained from a manufacturer. The Mayo-Gibbon was made by Custom Engineering and Development in St Louis, the DeWall machine was made by Travenol Laboratories in Illinois, and the Kay-Cross was made by Pemco Inc, in Cleveland.

Actually, very few of the Mayo-Gibbon machines were sold. It was too expensive and too complex. The Travenol disposable bubble oxygenator was the simplest and least expensive, but it was best used for short periods of time. Long perfusion with this system was thought to produce problems. The rotating disc oxygenator was a very reliable system, but it also had some disadvantages. It required a fairly large priming volume of fresh blood, which eliminated its use for emergency operations, and it required extensive cleaning and reassembly after each use.



**Figure 12.** The Kay-Cross rotating disc heart-lung machine manufactured by Pemco Inc. Standing by the machine is William Koteles, founder of Pemco. Used with permission from Pemco Inc.

In the 1960s, several more companies began to produce heart-lung machines. The film and disc oxygenators were gradually replaced by hard-shell disposable bubble oxygenators that contained a defoaming chamber and a heat exchanger. By the mid-1980s, hollow fiber micropore membrane oxygenators became available, and at present they are still the most common oxygenator in use.

The heart-lung machine was one of the most important surgical developments of the second half of the 20th century, and John Gibbon deserves the major share of credit for its success. His machine was designed to operate with as many safety and automated features as possible, which made it complex and expensive. Gibbon thought that the heart-lung machine would have limited usefulness. Certainly, he had no idea that hundreds of thousands of operations using cardiopulmonary bypass would be done each year. As cardiac surgery evolved from its shaky start, the technology shifted from a very complex machine to a more straightforward device designed to be managed by a full-time specialist, the perfusionist.

During the next 10 years, after the first operation using cardiopulmonary bypass, the operative mortality for open heart surgery rapidly decreased each year. Better oxygenators, better surgical techniques, better cardiology, and many other improvements brought the risk of death down to single-digit levels. However, no one from that era would have predicted that many cardiac operations today are done with a risk of death of <1 in 100.

The first successful open heart operation using cardiopulmonary bypass was done by John Gibbon on May 6, 1953. The operation was closure of an atrial septal defect. The patient, Cecelia Bavolek, was alive and well on the 50th anniversary of that operation in May 2003.

## Disclosures

None.

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