*Historical Perspectives*

# The Development of the Starr-Edwards Heart Valve

**Annette M. Matthews**

*Development of the Starr-Edwards heart valve marked a new era in the treatment of valvular heart disease. Until the development of the Starr-Edwards valve, there were no published reports of patients who had lived longer than 3 months with a prosthetic valve in the mitral position. This valve was the result of a unique partnership between a young surgeon, Dr. Albert Starr, and an experienced engineer, Mr. Lowell Edwards. Working as a team, these 2 men developed and successfully implanted the 1st Starr-Edwards valve within less than 2 years of their 1st meeting. Their key to success was their willingness and ability to make repeated modifications to their design to solve each clinical problem as it arose. Their constant focus on the clinical goal aided the rapid transformation of their design from a leaflet valve to a shielded ball valve, and finally to an unshielded ball valve suitable for implantation in a human being. Along the way, they abandoned the idea of imitating the appearance of native valves, in favor of developing valves that would be clinically successful. Their work has provided help and hope for patients who otherwise would have died from the complications of rheumatic heart disease and other valvular disorders for which valve replacement is the only treatment.* ***(Tex Heart Inst J 1998;25:282-93)***

Dr. Albert Starr recalls the day that he met Lowell Edwards:

> Lowell Edwards was an electrical engineer by training, who, in 1958 at the age of 65 years, stepped out of his Cadillac and into my office with an ambitious plan to build an artificial heart. He was well-versed in hydraulics and believed that the heart could easily be imitated. I thought he was 30 years too soon, and I convinced him to work on one valve at a time.[1]

In less than 2 years from the day they met, Dr. Starr and Mr. Edwards achieved the 1st successful replacement of a human mitral valve. Starr has called this his most memorable operation.[2]

By May of 1963, working on 1 valve at a time, Starr and Edwards had achieved the 1st successful triple valve replacement (aortic, mitral, and tricuspid) in a human patient—a man named Virgil Roberts. The cardiologist, Dr. Donald Sutherland, said of this success, "When Dr. Starr, at the next fall meeting of one of the thoracic surgery groups, began his talk on valve replacements with a slide of Virgil Roberts' x-rays, the people got up and clapped—I mean, a bunch of thoracic surgeons."*

## Albert Starr and Lowell Edwards

Albert Starr (Fig. 1) was born on June 1, 1926, in New York, New York. He received his Bachelor of Arts degree from Columbia College (now Columbia University) in 1946 and his Doctor of Medicine degree from Columbia's College of Physicians and Surgeons in 1949. He then went on to do his internship at Johns Hopkins Hospital and his residency in general and thoracic surgery at the Bellevue and Presbyterian Hospitals of Columbia University.[3] He was an assistant in surgery at Columbia University until 1957, when he moved to Oregon—having been enticed, in part, by the Oregon Heart Association's promises to help fund his research and to take him salmon fishing.** There he worked for the Crippled

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* Interview with Donald Sutherland, MD, 10 June 1998, Oregon Health Sciences University Oral History Project. Conducted by Linda Weimer, MLS, MPS.

** Interview with Howard Stroud, MPH, 17 August 1998, Oregon Health Sciences University Oral History Project. Conducted by Annette Matthews.

***Fig. 1*** *Albert Starr (ca. 1960).*
*(Courtesy of Oregon Health Sciences University)*

***Fig. 2*** *Margaret and Lowell Edwards (ca. 1960).*
*(Courtesy of Miles Edwards, MD)*

Children's Division at the University of Oregon Medical School (now the Oregon Health Sciences University).[4] Starr was an instructor in surgery when he met Lowell Edwards in September of 1958. Starr has said of this meeting, "He was in his 60s and I was in my 30s, but there was no generation gap between us."[5]

When Lowell Edwards met Albert Starr, Edwards (Fig. 2) was already semi-retired from a successful engineering career. Edwards was born in Newberg, Oregon; he was the son of a devout Quaker. His parents, Clarence Edwards and Abby Miles, owned a series of electric power companies. He attended Pacific College (now George Fox University) for 2 years, and then went to Oregon State College (now Oregon State University), where he met his wife, Margaret Watt, and graduated with a degree in electrical engineering. He learned hydraulics, mechanics, and design in his 1st job after college as a trainee with the General Electric Company in Schenectady, New York.[6]

Lowell Edwards' creativity and knack for invention were evident at an early age. His wife notes, "From the earliest childhood Lowell enjoyed making things, but invariably these things had to be something a bit different—something to surprise his parents or friends."[6] Before Edwards retired, he had patented more than 63 of his inventions, including a hydraulic tree-barking system for Weyerhaeuser Timber Company and a centrifugal high-altitude booster pump that Thompson Ramo Woodridge Corporation used in aircraft engines in World War II.[7,8] At one time, 85% of military airplanes were equipped with Edwards' patented pumps.[9] After Edwards retired, his interests turned to medical projects, including, in addition to the heart valve, a ballistocardiograph and a membrane oxygenator.

It has been said of the partnership between Dr. Starr and Mr. Edwards, "Dr. Starr provided the necessary knowledge of anatomy and cardiac physiology together with surgical skill for valve replacement. Mr. Edwards provided the knowledge and mechanical skill to transfer the concepts of need (into) the physical reality."[10]

## The Need for a Prosthetic Valve

Lowell Edwards' interest in working with the mitral valve is thought to have arisen from his childhood battle with rheumatic fever. Despite the decrease in deaths from rheumatic fever from 30/100,000 in 1940 to 12/100,000 in 1958, acute rheumatic fever and chronic rheumatic heart disease continued to be the most common causes of valve failure that necessitated valve replacement.[11,12] The most serious complication of rheumatic fever is valvulitis, the healing of which can lead to thickening, adhesions, and stenosis of the aortic and mitral valves.[13] The heart eventually becomes hypertrophic from the additional force required to pump the blood.[14] For the patient, this means ever-increasing shortness of breath and incapacitation. By the early 1950s, researchers had established the link between streptococcus A and rheumatic fever. The exact mechanisms of the development of rheumatic fever after an infection remain elusive to this day. Other causes of mitral

valve failure that lead to valve replacement include rupture of leaflets secondary to bacterial endocarditis, and congenital malformation of valves.[15]

Until the advent of the mitral valve prosthesis, the 2 major techniques used to palliate mitral stenosis were commissurotomy and finger dilation. Elliot Cutler and Samuel Levine performed the 1st commissurotomy in September of 1923 at the Peter Bent Brigham Hospital in Boston.[16] They called their procedure valvotomy, and used an instrument that they called a valvotome. Valvotomy involved "inserting a knife-hook (valvotome) into the apex or down the aorta and cutting or tearing out valve cusps." They performed this procedure 6 times between 1924 and 1928. This procedure transformed mitral stenosis into mitral regurgitation, but at that time mitral regurgitation was thought to be less damaging than mitral stenosis.[17]

Finger dilation was the other major technique used to repair mitral valve stenosis. In this technique, a finger or a knife was used to fracture the calcified mitral valve, so that it would enable blood to pass more freely. At Peter Bent Brigham Hospital, Sir Henry Souttar performed the 1st finger dilation, and his patient made an uninterrupted recovery. Souttar said of the operation:

> The information given by the finger is exceedingly clear, and personally I felt an appreciation of the mechanical reality of stenosis and regurgitation which I never before possessed. To hear a murmur is a very different matter from feeling the blood itself pouring back over one's finger. I could not help but be impressed by the mechanical nature of these lesions and by the practicability of their surgical relief.[18]

This procedure gave him, if nothing else, an appreciation of the mechanical nature of the valve and its lesion. Souttar performed the procedure only once, however, because as he explained in a letter to Dwight Harken many years later "the Physicians declared that it was all nonsense and in fact that the operation was unjustifiable." Souttar went on to say of the situation "In fact it is of no use to be ahead of ones time."[19,20]

Souttar's work was unknown to Charles Bailey and to the team of Harken and Ellis, who independently reinvented finger dilation in 1948. Bailey called his procedure commissurotomy, and Harken and Ellis called theirs valvuloplasty. Both procedures were conceptually the same as that developed by Souttar 25 years earlier—they involved the splitting apart of the valve commissures. The procedure then became widely used. Researchers such as Smithy, Murray, and Brock developed several variations on the surgical approach and technique of commissurotomy and valvotomy, but the problem remained that some valves were so badly stenosed that the only truly effective solution would be replacement of the valve itself.[21]

## Early Development and Placement of Prosthetic Heart Valves

The development of the ball-and-cage valve design is attributed to the patent of the bottle stopper in 1858 (Fig. 3). It is not clear what inspired Campbell and Hufnagel, but in the early 1950s each independently came up with the idea for a prosthetic heart valve that consisted of a cage and a mobile spherical poppet.[22] Hufnagel's valve was made of a Plexiglas (methyl methacrylate) cage surrounding a silicone-coated nylon poppet (Fig. 4).[23,24] Although Campbell never placed his valve in a human being, Hufnagel's valve was 1st implanted in a human patient in September of 1952; the valve was placed in the descending thoracic aorta using a closed procedure. Lefrak and Starr[22] have described the 1st human implantation of the Hufnagel valve as "igniting the fire of prosthetic valve implantation."

Hufnagel's demonstration that it was possible to place a mechanical valve in a human patient might have lighted the fire, but other historic and scientific advances made the early 1950s an opportune time for the development of the Starr-Edwards valve. In 1945, the end of World War II had resulted in the release of engineers and scientists for civilian research projects. The rise of industrial science during World War II had encouraged partnerships among scientists in different fields. Surgical techniques were improving and were being used to treat cardiovascular conditions like patent ductus arteriosus (1939), tetralogy of Fallot (1945), coarctation of the aorta (1945), pulmonic stenosis (1948), and mitral stenosis (1948).[25]

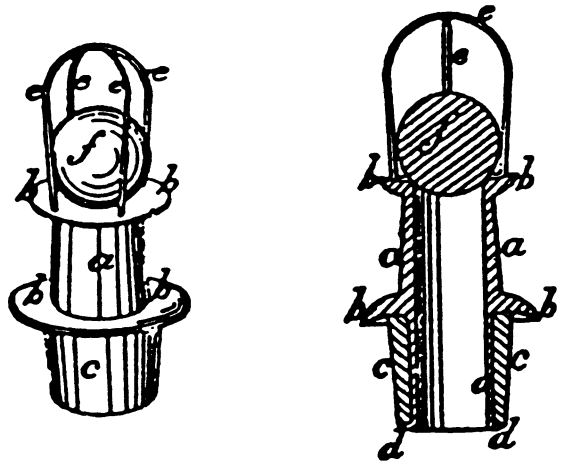

***Fig. 3*** *Williams' 1858 bottle stopper design (US Patent No. 19323), which uses the ball-and-cage principle.*

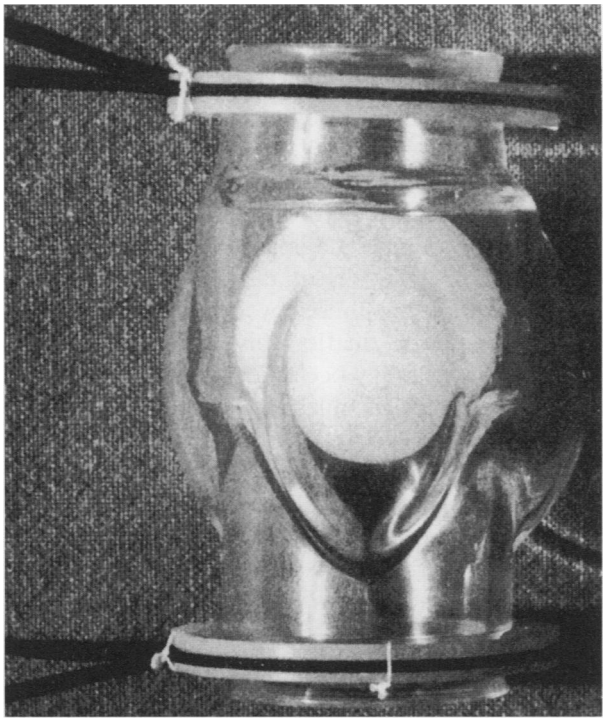

***Fig. 4*** *Hufnagel's aortic valve.*

*(From: Reardon MJ, et al. The evolution of aortic valve surgery.[23] Reproduced with permission.)*

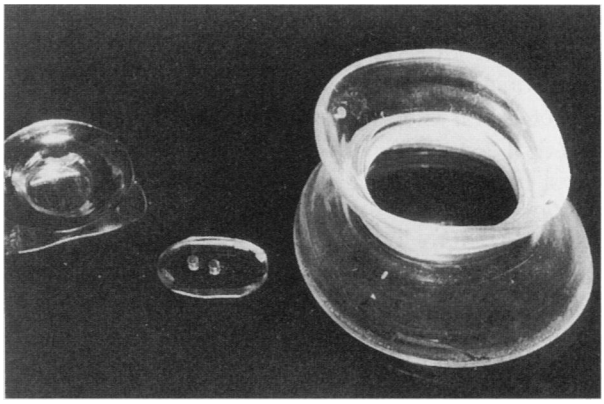

***Fig. 5*** *Chesterman's Perspex valve.*

*(From: Norman AF. The first mitral valve replacement. [letter][29] Reprinted with permission from the Society of Thoracic Surgeons.)*

In 1953, Gibbon became the 1st surgeon to successfully use the heart and lung machine on a patient, paving the way for the 1st open-heart operations.[26] In 1954, Lillehei introduced the idea of using blood from another patient to oxygenate the blood of a patient undergoing an open-heart procedure.[27] Also becoming available were new methods for evacuating air from the heart and new materials (Plexiglas, Teflon, and Dacron) that had been developed for other uses. Surgical experience with implantation of these materials, such as DeBakey's use of a Dacron prosthesis to correct an aortic aneurysm, was growing.[28]

The 1st placement of a ball valve in the mitral position in a human being has been attributed to Judson T. Chesterman.[29] The valve was made of Perspex, and consisted of an outer cage, a poppet, and 2 buttons used to fasten the valve to the outside of the heart (Fig. 5). On July 22, 1955, at the City General Hospital in Sheffield, England, Chesterman implanted the valve in a closed procedure; the patient lived for 14 hours after the valve was placed, but he died when the poppet twisted out of position.

Several groups of researchers had attempted to place mechanical mitral valves in human beings before the success of Starr and Edwards. These included groups led by Kay,[21] Braunwald,[30,31] and Ellis.[32] However, thromboembolism was a major obstacle:

> The great problem was not that they could not put in valves that would work, but that they always produced thrombi in dogs. This was true particularly at the junction between the myocardium or endocardium and the prosthetic substance. On the left side if these thrombi dropped off, the animal died of a cerebral embolism, and this inevitably took place within 3 or 4 weeks.[33]

In 1959, Lowell Edwards was asked how long it would be before a successful prosthetic heart valve would be a reality. He responded, "The need exists and it will eventually be met. That is the law that all nature follows."[34]

## Development of the Starr-Edwards Ball Valve

The development of the ball valve might have been a fulfillment of nature's law, but the valve was not natural in appearance. The ball valve has been described as "departing radically from the concept of artifice imitating nature," and Starr's work as "departing from nature's format."[33] Starr himself has described the ball valve as a "repugnant intracardiac appliance."[33] But Starr has also said,

> The artificial heart valve is definitely here to stay. We must think of it as an attempt to solve a clinical problem with wide ramifications. Our job is not to design a valve identical to nature's, not to see how close we can come to duplicating a natural phenomenon, but to overcome the clinical problem of the diseased heart valve. If we can do this with a valve similar to the natural one—fine. But we must evaluate on the basis of function rather than form.[35]

This ability to think of the mitral valve in terms of its function rather than its form was the major insight

that would be applied over and over again in the development of the Starr-Edwards valve. Its 1st application came after several months of work on a leaflet mitral valve. The leaflet valve (Fig. 6) consisted of 2 silicone-rubber leaflets that were hinged on a central crossbar made of solid Teflon; it included a Teflon cloth margin for fixation. The leaflet valves were plagued by thrombus formation. Thrombus would originate at the suture line and grow by direct extension onto the leaflets. In most cases, the valve became totally occluded after only 2 or 3 days.[36] After months of work, Starr and Edwards abandoned the leaflet valve to work on a ball valve. Edwards explained,

> There were a lot of us trying to build an artificial heart valve. Most of the teams felt that they had to copy nature, that the valve had to look like the original human valve. But the valves weren't working. Dr. Starr said, 'Let's make a valve that works and not worry about its looks.'[34]

A paper published in 1958 by Ellis and Bulbulian[37] provided another source of inspiration for a switch from the leaflet design to the ball design. In this paper, Ellis and Bulbulian described their results at the Mayo Clinic with a caged-ball prosthesis for mitral valve replacement in dogs. Ellis and Bulbulian had abandoned their attempts to develop the ball-valve design for a prosthetic mitral valve, because it, too, was prone to thrombosis. Starr and Edwards, however, saw the ball valve design as a solution to the problem of thrombus growing onto the occluding device. Because the ball was not fixed to the ring, the thrombus would not have a direct path on which to grow. The almost constant motion of the ball would result in a self-cleaning valve—the agitation of the ball would remove the thrombus as it formed.

In vivo testing of the early Starr-Edwards ball valves occurred in the dog laboratory at the University of Oregon Medical School. One of these dogs, a 70-pound Labrador retriever named Blackie, lived for 13 months with a ball valve in the mitral position.[38] But thrombus arising from exposed, damaged endothelium caused the deaths of many of the dogs. The thrombus would originate on the atrial aspect of the juncture with the mitral annulus, and would grow over the prosthesis by direct extension. In common with the leaflet valves, the ball valves would become totally occluded in 2 or 3 days. Also, postoperative anticoagulation therapy caused hemorrhaging. Hemothorax and infarctions of the small bowel and kidney were common causes of death.[39,40]

To solve the postoperative problems of thrombus formation and cardiac infarction in dogs, Starr and Edwards developed a ball valve with a Silastic shield that covered the area where thrombus had been forming (Fig. 7). Dr. Starr describes the day he thought of the Silastic shield:

> It was a beautiful spring afternoon. . . I was bounding up the steps of the Basic Science Building with my mind wandering aimlessly when it suddenly struck me that a Silastic shield over the area where the thrombus formed on the valve would give us a chance to have long-term survivors. . .[41]

The Silastic shield slowed the formation of thrombus, and gave the dog time to heal before anticoagulation therapy was begun.[39] The shielded valve yielded an 80% survival rate in dogs. After the development of the Silastic shield, "It wasn't long before there was a kennel full of dogs with mitral valve replacement thriving in the animal laboratory."[42] Although this shielded valve was really a dog valve and

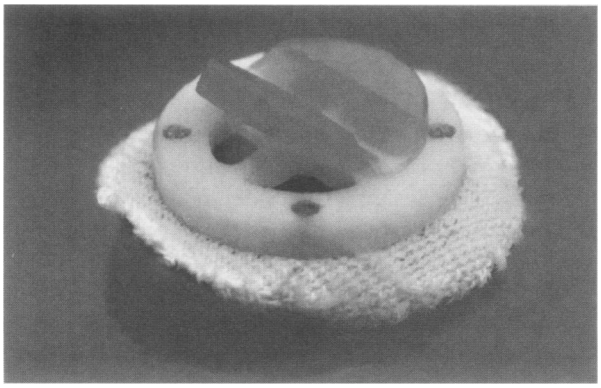

***Fig. 6*** *Early Starr-Edwards leaflet valve.*
*(Courtesy of Jeri Dobbs, PA)*

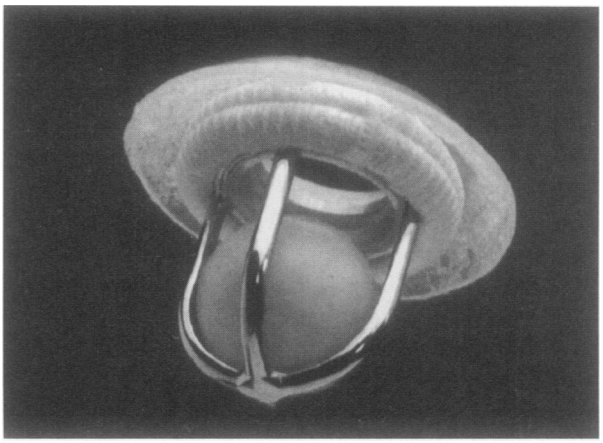

***Fig. 7*** *Ball-and-cage dog valve with Silastic shield.*
*(Courtesy of Jeri Dobbs, PA)*

not a human valve, it has been described as "the crucial link to the development of a safe caged-ball prosthesis for human application."[22] It was eventually marketed as a separate item to be used in research.[43]

Despite its history of thromboembolism, the non-shielded ball valve was chosen for placement in human beings. There were 2 reasons for this selection. First, human beings are less likely to develop thrombi than are dogs.[36] Denton Cooley said, "Humans will tolerate this surgery much better than dogs. . . . Dogs, for some reason, don't like to have their blood bubbled through a pump oxygenator."[44] Second, the non-shielded valve could be inserted more quickly and more easily than could a shielded prosthesis. Starr and Edwards commented,

> A great premium is to be placed on the speed and ease of insertion by conventional approaches with minimal surgical trauma. . . . While the shielded as well as the unshielded valve satisfy these criteria, the added simplicity of the unshielded valve led to its initial clinical trial despite the clotting problem it provided in the dog.[39]

The choice of the unshielded valve for placement in the 1st human patients shows, again, the ability of Starr and Edwards to emphasize the function of the valve over its form. In this case, the functional need for quick and easy placement in the human patient was the deciding factor for the selection of the unshielded valve.

At the conference on prosthetic valves in September of 1960, many valve designs were displayed, and some of them were strange and complicated, "like man's early attempts to make a flying machine."[9] At this conference, the valve designs showed a trend toward imitation of native human valves.[22] Starr presented the experience with his ball-valve prosthesis, describing his single attempt to place the valve in a human patient and the death of that patient 10 hours later from air embolism.[5,45] The chairman of the conference, K. Alvin Merendino, said at the conclusion of the conference, "Unfortunately no one unveiled *the valve*." Ten days later, Albert Starr became the 1st physician to successfully implant *the valve*.[22]

The 1st Starr-Edwards valve to be successfully implanted in a human patient was modeled after the valve designed by Ellis and Bulbulian. It had a methyl methacrylate (Lucite) cage with thick struts and a machined ring orifice. A compression-molded silicone-rubber ball was placed inside the cage and the ring was then solvent-welded to the cage with acetone (Fig. 8). This valve was available for human trial in July of 1960; it was 1st placed in a human patient on August 25, 1960.[33]

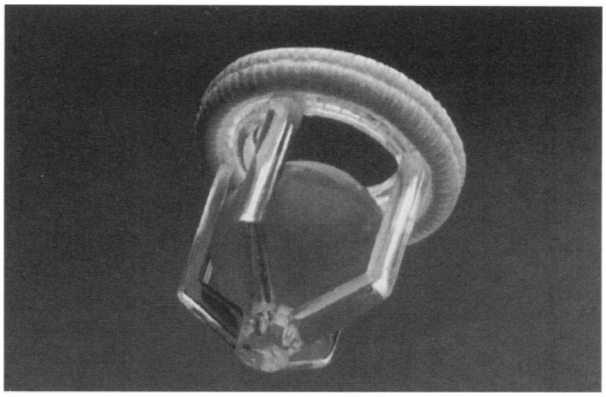

***Fig. 8*** *Starr-Edwards ball valve with Lucite cage and compression-molded silicone-rubber ball.*

*(Courtesy of Howard Stroud, MPH)*

The earliest mitral prostheses were the Model 6000 series; they went through several stages of development (Figs. 9 and 10). In 1967, Dwight Harken[19] described his famous "Ten Commandments" for the development of a prosthetic heart valve. In 1968, engineers from Edwards Laboratories[46] described their own "Nine Commandments" for the development of a prosthetic heart valve. The 9 "commandments" were:

- *Embolism Prevention.* The most difficult problem was still thromboembolism.
- *Durability.* Durability and corrosion resistance had been improved by forming the struts from stainless steel instead of Lucite.
- *Ease and Security of Attachment.* Ease and security of attachment had been improved by changing the shape of the sewing ring from that of a doughnut to a flange; the new shape allowed greater contact with the annulus.
- *Preservation of Surrounding Tissue Function.* Preservation of surrounding tissue function had been improved via 2 modifications: the profile of the cage was made rounder where it had previously been conical, and a porous silicone-rubber sponge was inserted into the body of the sewing ring to provide flexibility and an antibiotic reservoir.
- *Reduction of Turbulence.* Turbulence had been reduced by increasing the orifice-to-ball ratio.[36]
- *Reduction of Blood Trauma.* The mesh size of the Teflon fabric was enlarged to encourage neointima formation and to reduce blood trauma.
- *Reduction of Noise.* Hufnagel's early valves had a nylon poppet that made a distinct clicking noise that was audible to the patient and to people around the patient. Hufnagel later covered the poppet with silicone to reduce the noise.[24] The poppet of the Starr-Edwards valve was made of a solid piece of compressed silicone. The Starr-

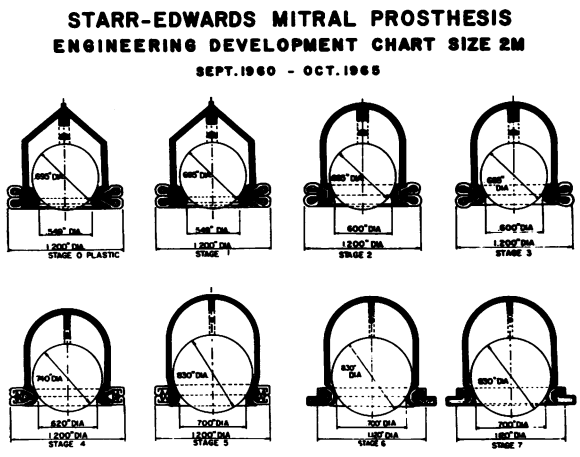


***Fig. 9*** *Engineering development chart for the Starr-Edwards mitral valve prosthesis.*

*(From: Starr A, et al. The present status of valve replacement.[12])*

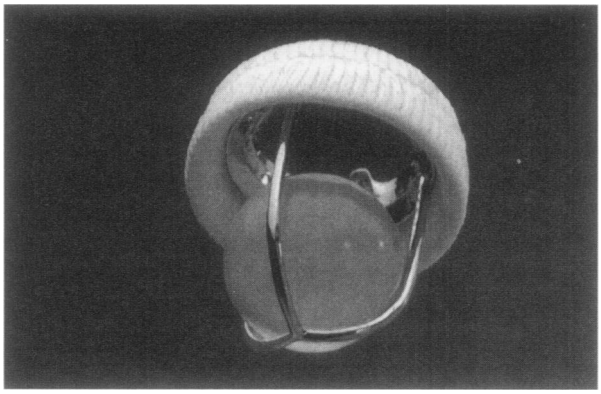

***Fig. 10*** *Starr-Edwards ball valve with metallic cage.*

*(Courtesy of Adnan Cobanoglu, MD)*

Edwards valve was quieter than Hufnagel's valve, but it could still be heard in thin-chested people if the observer placed his or her ear a few inches away from the patient's naked chest.[47]

- *Use of Materials Compatible with Blood and Tissue.* All of the materials used by Starr and Edwards had been shown to be nonreactive with blood and tissue. These materials included Stellite 21 (a mix of cobalt, chromium, molybdenum, and nickel), Teflon cloth, Teflon suture, methyl methacrylate, stainless steel type 302, and compression-molded silicone rubber.[36]
- *Development of Methods of Storage and Sterilization.* For sterilization, the valve was cleaned with detergent and autoclaved before it was implanted in the patient. The valve could be stored and autoclaved again, if necessary.[43]

In March of 1965, Model 6120 was created. The struts of this valve were thinner than those of previous models, and the sewing ring was extended over the inflow face of the valve. Barium sulfate was embedded in the poppet to make it radiopaque. While additional modifications were attempted, including a valve completely covered in cloth, and a valve in which the ball ran along a metal track, the Starr-Edwards Model 6120 valve was used widely, in virtually unchanged form, for more than 20 years.[48]

Lefrak and Starr[36] have commented on the speed with which the Starr-Edwards valve was developed:

> Lowell Edwards' determination and financial backing supported the provision of new models for animal implantation every few weeks or months, allowing the screening of a large number of designs in a short period of time.

Much of the initial financial backing came from Edwards himself, but other individuals from various corporations also provided materials and techniques. Silas Braley of Dow-Corning supplied silicone rubber and other silicone products used in the fabrication of the prosthesis. Norman Jeckel of U.S. Catheter and Instrument Company provided Teflon products used to make the fixation ring. R.R. Miller of Precision Metalsmiths Inc. helped to solve problems with casting techniques.[39] The Oregon Heart Association provided financing for additional equipment and supplies for the early valve replacements; the association funded the purchase of heart-lung machines for the dog laboratory and for the operating suites at the University of Oregon Medical School, and the purchase of many of the black Labrador retrievers used to test the prototype valves.*

The close proximity of Edwards' laboratory to his home probably contributed to the speed with which the early valves were developed. The early prototypes of the Starr-Edwards ball valves were manufactured in the work-shed of a cabin near Mount Hood, where Lowell Edwards and his wife spent their summers. Margaret Edwards recalled the time during the development of the valve:

> The Edwards family had bought a summer home on the Sandy River, forty miles east of Portland. Lowell was never happy far from his tools, so he had built a small laboratory there. It was in the small yellow building on the banks of the river that Lowell set to work on an artificial mitral valve. . . . After a year's work, valves were ready to try on dogs at the medical

*Interview with Howard Stroud, MPH, 17 August 1998, Oregon Health Sciences University Oral History Project. Conducted by Annette Matthews.

school. The results were more encouraging than they had expected.[6]

These encouraging results brought about "more hours of painstaking work. Often, waking at night, Margaret saw the tall trees of the forest illuminated by the lights from Lowell's workshop and she knew he was out there trying out yet another idea."[6] Work on the valves alternated between the Edwardses' summer home in the Mount Hood cabin and a workshop at the Edwardses' winter home in Santa Ana, California.[38]

Edwards originally thought he would make only a few experimental valves. When the valve proved successful, the demand was greater than he could satisfy on his own.[8] Edwards Laboratories was established in Santa Ana in 1961, to meet the increasing demand for Starr-Edwards valves.[9] The 1st home of Edwards Laboratories was a 40- x 60-foot rented building on Alton Street. The valves were produced by means of a wax casting process. By 1963, outside foundries were producing the castings. Wax molds were manufactured in Portland and individually packed and shipped to Precision Metalsmiths Inc. in Cleveland for casting.[38] Testing of the valve included accelerated fatigue testing, during which the valve was opened and closed 6,000 times per minute to simulate 43 years of wear (Fig. 11).[8] The lab was described as having a "science fiction atmosphere about it."[34]

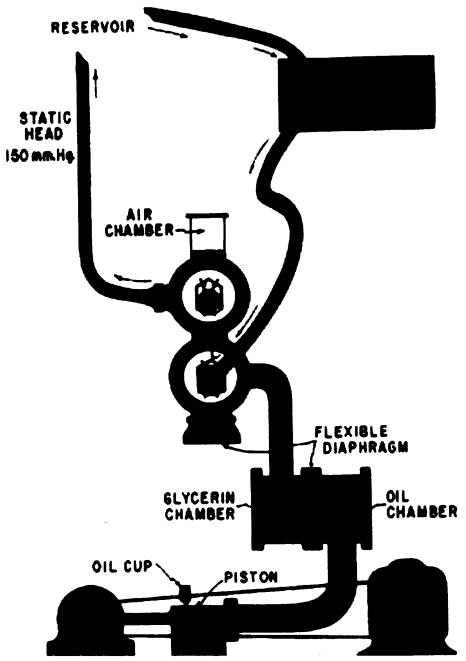


***Fig. 11*** *Accelerated fatigue pump.*

*(From: Starr A, et al. Mitral replacement: late results with a ball valve prosthesis.[49])*

## The 1st Eight Patients

William C. Roberts, editor of *The American Journal of Cardiology*, describes the year 1960:

> 43-year-old John Fitzgerald Kennedy was elected president of the USA; 16-year-old Bobby Fischer successfully defended his US chess championship; *To Kill a Mockingbird* by Harper Lee and *The Rise and Fall of the Third Reich* by William Schirer were published; birth control pills were made available to the public; Polaris missiles were successfully fired from a submerged atomic submarine; the International System of Units (SI), based on the metric system, was adopted as a worldwide standard at a General Conference on Weights and Measures; Theodore Maiman, physicist, developed the first LASER (Light Amplification by Stimulated Emission of Radiation), and successful, i.e., prolonged survival, cardiac valve replacement occurred.[50]

It was a time "before the age of computers, before man had set foot on the moon, when biomedical engineering was still unheard of! Artificial heart valve operations were written up in the newspapers as the latest 'gee-whiz' items."[51] Development of the Starr-Edwards valve marked a new era in the treatment of valvular heart disease.[42] Before the Starr-Edwards valve was successfully placed in a human patient, there had been no successful replacements—no patients had lived longer than 3 months.[33,52]

Starr and Edwards[33] published their landmark paper on their experience with the Starr-Edwards heart valve in 1961. The information was 1st presented in a meeting of the American Surgical Association held on March 21-23, 1961. The paper describes the cases of the 1st 8 patients who received the Starr-Edwards heart valve, and it reveals that 6 of these 8 patients were still living at the time the paper was published—1 had lived as long as 6 months. The 1st successful mitral valve replacement had been achieved.

The 1st 8 recipients of the Starr-Edwards valve had suffered from severe, progressive rheumatic valvular disease. All were in New York Heart Association (NYHA) functional class III or IV, and most had severe cachexia and marked weight loss.[53] All had low cardiac output, pulmonary hypertension, and left atrial hypertension. At that time, the procedure was "indicated only in severely incapacitated patients with operative findings of a hopelessly damaged valve not amenable to any plastic procedure and in whom operation cannot reasonably be postponed."[33] As Edwards said, "Patients were ready to die or we weren't allowed to work on them."[34]

Support for the placement of the valve in a human patient came from Herbert Griswold, who was

then Chief of Cardiology at the University of Oregon Medical School. Dr. Griswold selected the 1st patients to receive the Starr-Edwards valve,[36,54,*] and his support, despite the death of the 1st patient, was a major reason that the placement of the experimental heart valve did not go the way of other new procedures, such as Sir Henry Souttar's valvotomy. Dr. Starr has said that "Dr. Herbert Griswold, Chief of Cardiology, and Dr. J. Engelbert Dunphy, Chairman of the Department of Surgery, were very supportive; the former by encouraging our 1st clinical use of the valve, and the latter by paving the way for our presentation at the next meeting of the American Surgical Association."[5]

Patients who were not considered for early valve replacement included those who had severe renal disease that was unrelated to cardiac failure, and those who had very advanced pulmonary emphysema, recent myocardial infarction, or other medical problems that limited the prognosis to such an extent that valve disease was only an incidental part of the problem.[12] Patients were candidates for the artificial valve only if no other procedure, such as commissurotomy, would work.[12,47] "During surgery, careful inspection of the patient's own valve is first made. If it indicates extensive calcification and inflexibility (most common cause: rheumatic fever) irreparable by any other known method, the mitral valve is removed."[8]

The 1st human recipient of a Starr-Edwards prosthetic mitral valve was a 33-year-old woman. She had already undergone a closed mitral commissurotomy and an open implantation of an artificial Ivalon mitral leaflet. She died suddenly 10 hours after her surgery while being turned in bed. Air trapped in her right pulmonary veins had embolized to her brain.[36,55] After her death, new procedures were developed to protect against air embolus. These included flooding the operative field with carbon dioxide[5,33] and using antifoaming agents such as Antifoam A.[55]

The 2nd patient, Philip Admunson, received the Starr-Edwards mitral valve on September 21, 1960 (Fig. 12). He had undergone 2 previous commissurotomies and was in NYHA functional class IV. Fibrosis and calcification had completely destroyed his mural leaflet, and his aortic leaflet was massively calcified and thickened to 1 cm.[33] Admunson was the 1st of the 8 patients to live more than 3 months with the Starr-Edwards mitral valve, and his operation is known as the 1st successful mitral valve replacement in a human patient.[33] Admunson survived for 15 years after the implantation of the Teflon and silicone Starr-Edwards valve; he died after falling from a ladder while painting his house.[34]

*Interview with Herbert Griswold, MD, 21 July 1998, Oregon Health Sciences University Oral History Project. Conducted by Joan Ash, PhD.

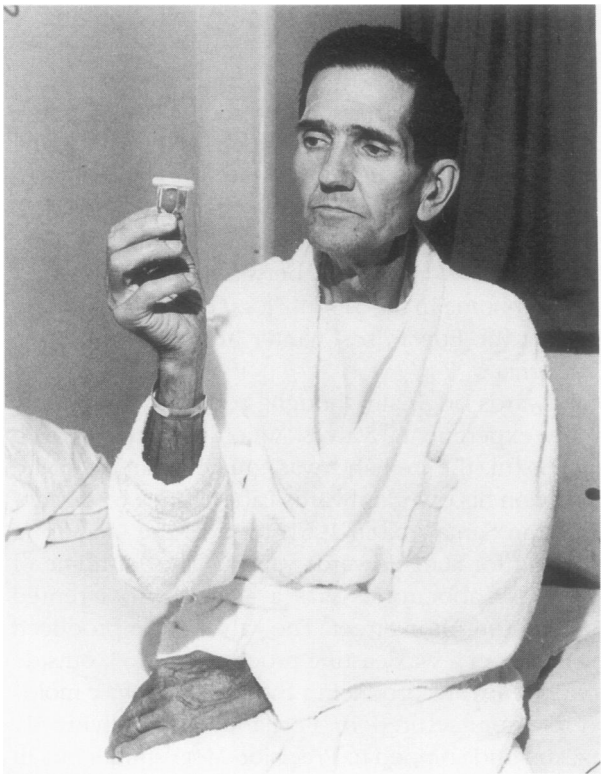

***Fig. 12*** *Philip Admunson, the 2nd human recipient of a Starr-Edwards mitral valve.*

*(Courtesy of Oregon Health Sciences University)*

The 3rd patient to receive the Starr-Edwards mitral valve was Amanda Dao (Fig. 13) . She had grown up in China, and was a scholarship student at the University of Oregon. A writer for *McCall's* magazine described the scene at her operation:

> Twenty-three men and women worked with such skill and coordination that the surgery was, in a medical sense, like an incredibly complex ballet. After the chest cavity was opened and the heart lung machine took over, bypassing the patient's heart, Doctor Starr entered the left ventricle chamber to attempt a relatively simple mitral repair—cutting away the calcified deposits that immobilized the opening. It was no use. The tissue was scarred and rigid beyond redemption. Amanda would have to have the artificial valve—or nothing.[54]

Before the operation, Mrs. Dao was unable to climb the stairs to her 3rd-floor apartment. After she had recovered from surgery, Mrs. Dao went to work in an oriental art shop in San Francisco and was able to run the 3 flights of stairs up to her apartment.[54]

In this 1st series of 8 patients who received the Starr-Edwards valve, all of the survivors experienced dramatic improvements. Heart size was reduced and

***Fig. 13*** *Amanda Dao, the 3rd human patient to receive a Starr-Edwards valve.*

*(Courtesy of Oregon Health Sciences University)*

murmurs often disappeared—replaced by the soft click of the new valve.[5] These patients began anticoagulation therapy on the 7th postoperative day, and would continue this therapy for the rest of their lives.[47] At that time, there was still a question about the need for long-term anticoagulation in human recipients of prosthetic valves.[10] Beginning in January of 1961, there was an "epidemic of staphylococcal infections involving other cardiac surgical patients and requiring temporary closure of the operating suite."[33] Penicillin-resistant staphylococcal septicemia eventually took the lives of at least 2 of the 1st 8 patients.[49]

Comments after the presentation of the manuscript suggest a mixture of disbelief and surprise.[5] Dr. Michael E. Debakey said, ". . . it seems to me that this is very impressive work on the part of . . . Starr and Edwards. Everyone who is familiar with this area of pathology and with the problems relating to correction of this type of lesion knows the difficulties involved in attempting to replace the mitral valve."[33] Dr. George H.A. Clowes, Jr. said, "This is a most remarkable piece of work, to have had 6 out of 8 patients survive."[33]

The work created its own media frenzy. The following headlines appeared in newspapers and magazines: "Miracle Heart Surgery Success," "Ball-Valve Mitral Implants Succeed: Seven Patients Alive Up to Seven Months," Heart Surgery Patient to be Truly Thankful on Thanksgiving."[9] People came from all over the world to have their valves replaced,

> and we actually had people come here—"we," Dr. Starr—had people come from Boston to do their heart surgery. We had people come from England, from India—literally from all over the world. That didn't last very long; it was a year or 2 until other people "caught up" and understood how to do these things.*

News of the valve's success also swept through the medical community. Between the time that the paper was presented in March of 1961 and the time it was published in October of 1961, institutions across the country began to perform the procedure.

George Siposs, an early engineer for Edwards Laboratories, recalls the experience:

> One of my most exhilarating experiences was listening with a stethoscope to the chest of a patient who had one of my valves implanted in the morning. Day by day the impossible became reality. It was exhilarating because the lead time from concept to product was so short.[51]

### The Starr-Edwards Valve Today

Today it is estimated that more than 175,000 patients have received a Starr-Edwards heart valve in the mitral, aortic, or tricuspid position.[5] The St. Jude mechanical leaflet valve is currently the mechanical valve of choice for mitral valve replacement in the United States.[56] Starr continues his research in heart valve prostheses. Lowell Edwards is dead, but several valves developed by the Baxter Healthcare Corporation carry his name, including the Carpentier-Edwards tissue valve.

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* Interview with Donald Sutherland, MD, 10 June 1998, Oregon Health Sciences University Oral History Project. Conducted by Linda Weimer, MLS, MPS.

lated to Albert Starr and the Starr-Edwards valve. Miles Edwards provided many difficult-to-find or out-of-print references. In addition, many physicians and researchers from Oregon and Texas deserve thanks for sharing their thoughts and memories regarding the development of the Starr-Edwards valve.

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