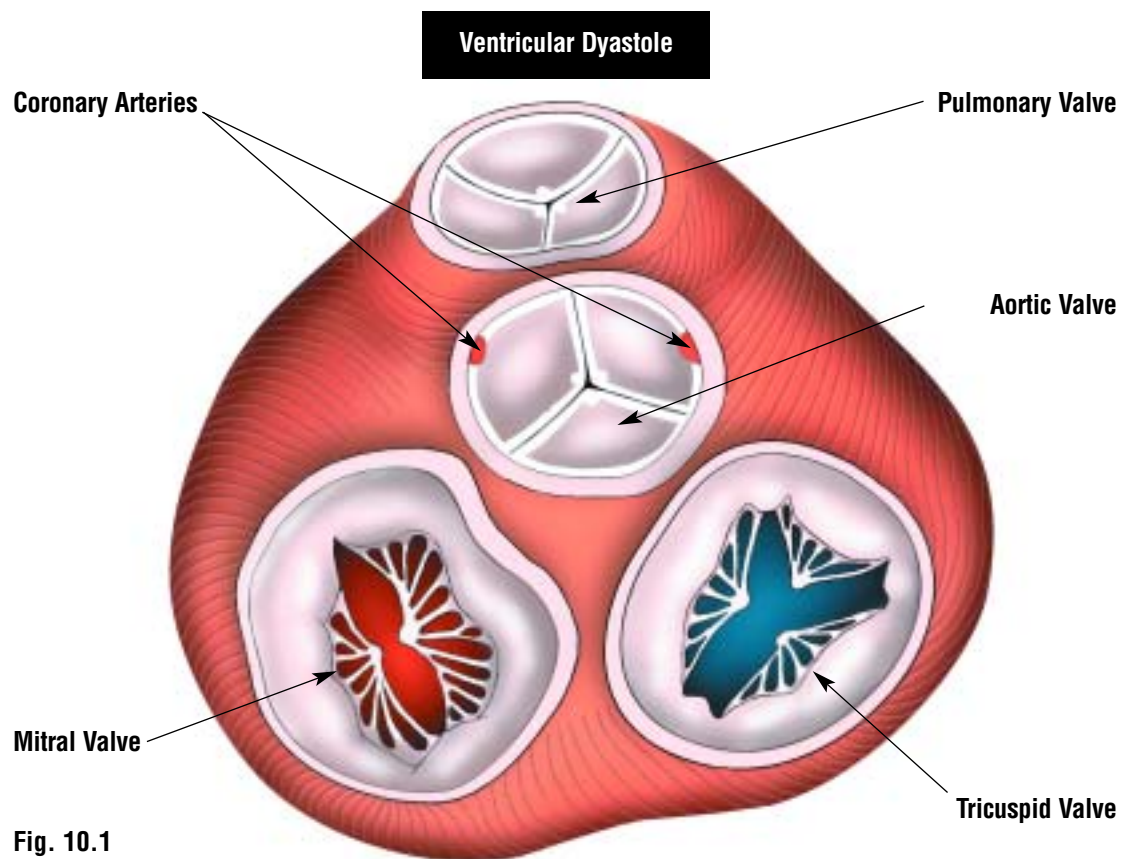
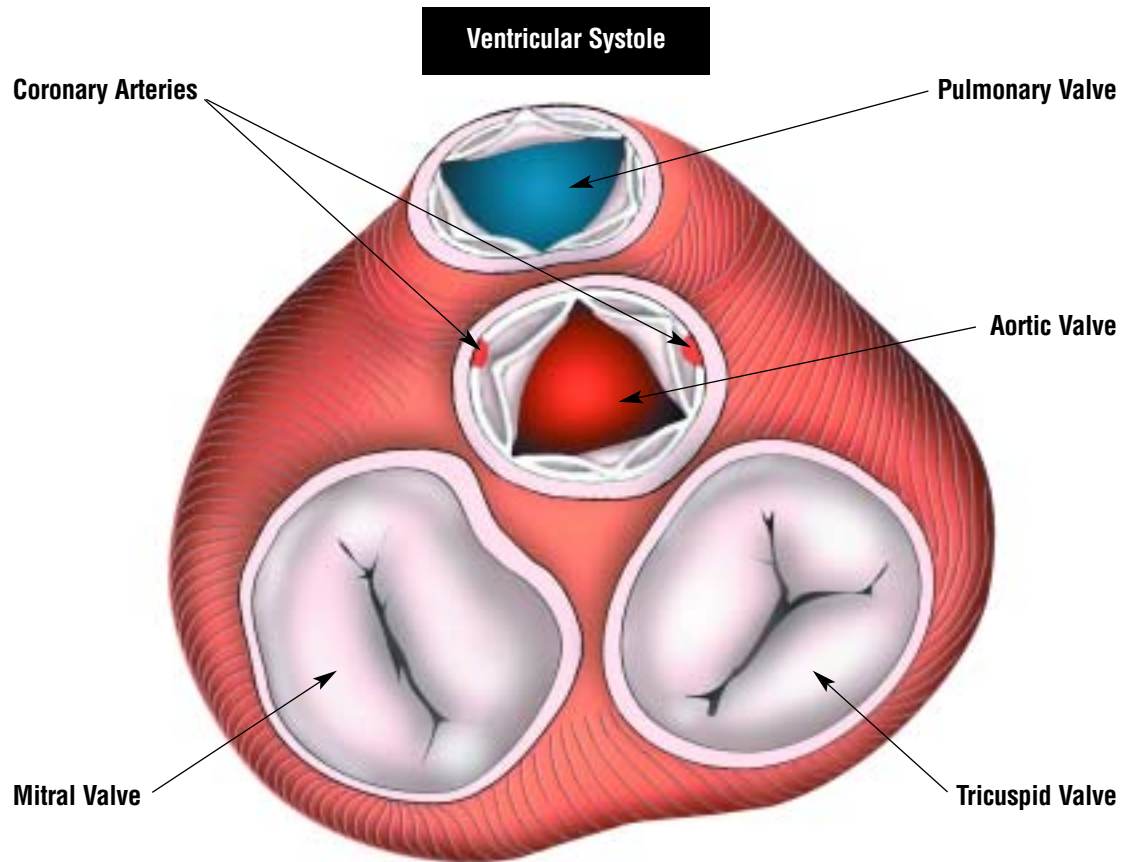


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**Fig. 10.1:** All four heart valves are seen from above here. The pulmonary valve is seen on top with the aortic valve immediately below it. The two red dots depict where the coronary arteries originate in the aorta just above the aortic valve. The two lower valves are the tricuspid, on the right, and the mitral valve on the left. The two illustrations show the valves during two stages of the heart cycle.

**Fig. 10.1**

# HEART VALVE PROBLEMS

**P**ICTURE A RED BLOOD CELL TRAVELING through the venous system toward the heart. It enters the heart through one of two major veins, either the superior vena cava or the inferior vena cava, and passes into the right atrium. The one-way tricuspid valve opens, and the cell flows into the right ventricle. The tricuspid valve is composed of three leaflets that are connected on their underside (right ventricle side) to string-like structures called **chordae tendineae**, which are connected to muscles called **papillary muscles**. The papillary muscles are outgrowths of the muscular right ventricular wall.

As the right ventricle contracts, the tricuspid valve closes and the pulmonary valve opens, allowing the blood cell to be pumped, or propelled, into the pulmonary artery, which channels unoxygenated blood containing carbon dioxide to the lungs. Like the tricuspid, the pulmonary valve is one-way and composed of three leaflets (also called cusps), although the leaflets differ from those of the tricuspid valve in shape. They look like three small cups. The pulmonary valve does not have chordae tendineae or papillary muscles.

After giving off carbon dioxide and picking up oxygen in the lungs, the newly oxygenated red blood cell returns to the

heart through one of the pulmonary veins and into the left atrium. The two-leaflet mitral valve opens, and the cell travels into the left ventricle. Like the tricuspid, the mitral valve has chordae tendineae, which are attached to papillary muscles. When the mitral and tricuspid valves are closed, the valve leaflets look like a parachute, and the chordae tendineae resemble the cords that connect the parachute to the jumper. The papillary muscle is the jumper.

When the left ventricle contracts, the aortic valve opens, allowing the red blood cell to stream out the aorta and into the arterial system that nourishes the body (see Fig. 10.1 for cardiac cycle). The two coronary arteries branch off the base of the aorta (aortic root) just above the aortic valve leaflets.



## Before the Heart-Lung Machine:

### *Opening Narrowed Valves*

The first attempt to open a stenotic (narrowed) heart valve in a human was carried out by Dr. Theodore Tuffier, a French surgeon, on July 13, 1912. After opening the patient's chest, he supposedly pushed the wall of the aorta near the heart through the stenotic aortic valve

**Chordae Tendineae:** String-like attachments that are part of the mitral and tricuspid valve apparatus that connects the valve leaflets, or flaps, to the papillary muscles on the ventricular wall.

**Papillary Muscles:** Tiny muscles located in the left and right ventricles that are attached by chordae tendineae to the mitral and tricuspid valves. These muscle structures help control the valve function.

and dilated the valve. The patient survived and was reported to be improved.

About ten years later, Dr. Elliot Cutler, a surgeon at Harvard Medical School, in collaboration with Boston cardiologist Samuel Levine, worked out a procedure to dilate the mitral valve. Their first patient was a desperately ill twelve-year-old girl whose mitral valve had been badly damaged and narrowed from rheumatic fever. She underwent successful mitral valve dilatation on May 20, 1923. Unfortunately, most of Cutler's subsequent patients did not survive the surgery, and he abandoned the procedure.

These sporadic and mostly unsuccessful attempts ceased by 1929, and things remained quiet until 1945, when Dr. Charles Bailey and his team again attempted to treat mitral valve **stenosis**. The first of their five human patients was a thirty-seven-year-old man who was operated on on November 4, 1945. He bled to death in the operating room during the procedure. The second patient was a twenty-nine-year-old woman operated on on June 12, 1946. Her condition improved for the first thirty hours after the

surgery but suddenly deteriorated, and she died forty-eight hours after the surgery. After these two failures, Bailey's home base, Hahnemann Hospital in Philadelphia, refused to allow him to attempt any more mitral valve dilatations. He even became known as the "butcher" of Hahnemann Hospital.

Their third patient, who was treated at a different hospital, was a thirty-eight-year-old man operated on on March 22, 1948. The surgery seemed to go well, but the patient hemorrhaged into the chest cavity on the second postoperative day. He died of complications. Patient four was a thirty-two-year-old man who underwent heart surgery on June 10, 1948. His heart stopped while the incision was being made to start the surgery. He could not be resuscitated and died in the operating room.

The surgical team then immediately regrouped and rushed to Episcopal Hospital, where the fifth operation, this one on a young woman, was started before the bad news from that morning was known and the hospital administration could forbid the procedure. Her mitral valve dilatation was successfully completed. One week later, Bailey brought the patient by train one thousand miles to Chicago, where he presented her to the American College of Chest Physicians annual meeting. She was without symptoms after the surgery and felt better than she had been feeling for years.

On June 16, a few days after Bailey's success, Dr. Dwight Harken in Boston successfully performed his first mitral valve dilatation. Three months later, Sir Russell Brock in England did his first successful similar procedure but did not report it until 1950, when he described six additional successful attempts.

#### *Targeting the Pulmonary Valve*

On December 4, 1947, Dr. Thomas Holmes Sellers, an English surgeon, completed the first successful surgery on a

#### **Stenosis:**

An abnormal narrowing of an orifice, blood vessel, or heart valve.

Dr. Elliot Cutler (below) performed the first successful mitral valve dilatation. His patient, a 12-year-old girl (right), had suffered from rheumatic fever. Her surgery was successful.





narrowed pulmonary valve. The surgery occurred during an operation for a congenital heart defect called **tetralogy of Fallot**. In this condition, there is an obstruction of blood to the lungs and a hole in the heart. This particular patient also suffered from advanced tuberculosis of both lungs. When Sellers opened the sac around the heart, he could feel the narrowed pulmonary heart valve each time the right ventricle contracted. He passed a special type of knife through the wall of the right ventricle and made slits in the narrowed valve. The patient made a good recovery and was markedly improved.

#### *The Development of Valve Replacement Surgery*

Like all forms of heart surgery, valvular surgery made great leaps forward as the heart-lung machine came into use. Doctors who had once only imagined the day when diseased valves could be replaced began to actually work to develop implantable valves. Artificial valves were

not a novel idea. The first ones had been developed in the 1950s, when Drs. Charles Hufnagel in Washington, D.C., and J.M. Campbell in Oklahoma independently developed and implanted artificial valves in the descending aortas of dogs. This could be done before the heart-lung machine because the descending aorta is far enough away from the heart. The surgeon merely placed clamps several inches apart on the aorta to interrupt blood flow, opened the aorta, inserted the artificial valve, and then stitched the aorta closed.

These two valves, which were called “cage-ball valves” because of their design, looked similar. After presenting this mechanical heart valve technique in animals at the American College of Surgeons annual meeting in 1949, Hufnagel began to use this procedure in human patients suffering from aortic valve incompetence. The valve implantation did not actually replace the patient’s own leaky aortic valve but acted as a supporting or auxiliary valve.



#### **The Advent of the Heart-Lung Machine**

Once the heart-lung machine was developed, surgeons began to attempt heart valve replacement with cage-ball valves. The first successful valve replacement was performed by Dr. Dwight Harken and his colleagues at Harvard’s Peter Bent Brigham Hospital in Boston. Harken used a cage-ball valve to replace the aortic valve. Many of the techniques described in his 1960 report are similar to those used today for aortic valve replacement.

The same year, Dr. Albert Starr successfully replaced the mitral valve by using a cage-ball valve.

In 1964, Starr and associates reported on thirteen patients who had undergone multiple heart valve replacements. One patient had the aortic, mitral, and tricuspid valves replaced on February 21, 1963.

By 1967, nearly two thousand Starr-Edwards heart valves had been implanted, and the cage-ball prosthesis had gen-

In 1960, Dr. Dwight Harken (left) performed the first successful valve replacement in the normal aortic valve position with an artificial valve. He used a cage-ball valve to replace the aortic valve.

#### **Tetralogy of Fallot:**

A set of four individual defects, including: 1) a ventricular septal defect; 2) an obstruction of blood flow from the right ventricle to the pulmonary arteries; 3) overriding of the aortic valve above the ventricular septal defect; and 4) an abnormally thickened right ventricle.

## **ALBERT STARR AND THE STARR-EDWARDS HEART VALVE**

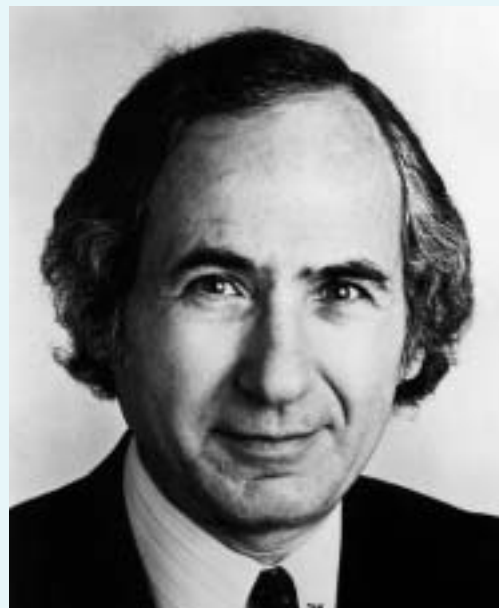
Dr. Albert Starr (right) was part of the team that developed the Starr-Edwards cage-ball heart valve (facing page). Starr was the first to successfully replace a mitral valve with that valve. The Starr-Edwards valves went on to become the world standard.

**A**FTER GRADUATING FROM Columbia College of Physicians and Surgeons in 1949, Dr. Albert Starr served a one-year internship at Johns Hopkins Hospital. There, he worked under the world famous surgeon Dr. Alfred Blalock, who had pioneered the Blalock-Taussig operation for children with cyanotic heart disease.

When his internship was completed, Starr returned to New York but was soon drafted into the U.S. Army Medical Corps to serve first as a battalion surgeon in the First Cavalry Division in Korea, then as a surgeon for a Mobile Army Surgical Hospital (MASH) unit. In a single year, he performed more than one thousand major operations.

“Korea was the first war in which you had an almost unlimited backup system to a limited war,” Starr said in a recent interview. “It was a war in which there was almost an unlimited supply of human blood available for transfusion on the battlefield. There was also the beginning of antibiotics, and helicopter evacuation so that someone wounded in a firefight in Korea would be back in a MASH within minutes of being wounded, rather than hours or days. The survival rate, if you made it back to the MASH hospital, was about 95 percent.”

After his tour of duty, he returned to complete his surgical training at Bellevue and Presbyterian hospitals in New York. By 1957, Starr had finished his thoracic surgery residency and moved to the University of Oregon, Portland, to start



**Albert Starr**

an open heart program. This is where Starr was first exposed to heart valve surgery and the problems surgeons were having repairing diseased valves. After experimenting with all sorts of valve prostheses, Starr became convinced that valve replacement was necessary to save many patients with diseased mitral valves because there was no way to repair badly deformed and diseased mitral valves.

Enter a retired engineer named M. Lowell Edwards. A successful and independently wealthy engineer, Edwards had several important inventions to his credit and originally approached Starr to help him develop an artificial heart.

“I thought he was overreaching, to put it mildly,” Starr said. “What I discovered was that he was a very suc-

successful engineer, and although he was wearing the typical Oregon golfer's dress, he was very accomplished and had numerous inventions to his credit. One of them was a fuel injection system for rapidly climbing aircraft during World War II. The P-38 and many of our fighter aircraft had his fuel injection system, and a good part of the successful war effort, at least as far as the air war is concerned, is credited to his fuel injection system. In the Battle of Britain, the Spitfires had his fuel injection system, and that enabled them to get up to very high altitudes very rapidly without the system failing."

When Starr pointed out that medicine didn't even have artificial valves yet, much less an artificial heart, the two decided to begin one valve at a time and invent prostheses. They started with the mitral valve and considered every kind of valve known. After drifting from valve to valve, they finally hit upon the ball valve, which showed early promise because it was not as easily occluded by the blood clots that quickly formed around the sutures of more conventional leaflet-type valves.

They quickly learned, however, that blood clots did form in the ball valves — it just took longer before the clot was large enough to block up the free-moving ball. At the time, they were performing their early experimentation in dogs, many of whom were dying from thrombosis months after their valves were implanted. This challenge led Starr and Edwards to the silastic shield, which was basically a retractable diaphragm that covered the sutures and prevented blood clots from forming. This shield created long-term survivors, and soon Starr had a kennel full of active dogs that had undergone mitral valve replacement.

"The chief of cardiology, Dr. Herbert Griswold, knew we had a kennel full of

active dogs and came to visit us in August 1960. He looked at all these dogs and said, 'Starr, we have to do this clinically.' That was the first time we began to think about that seriously because I thought it would be a couple years' project at least."

Interestingly, the first valve implanted in a human did not use the silastic shield. Starr, knowing that dog's blood clots very aggressively, figured he wanted the simplest procedure possible and, if the patient's blood clotted, they could always administer anticoagulant medication. This first operation was done in September 1960 on a young woman in her mid-twenties. The Starr-Edwards cage-ball valve prosthesis quickly became established as the gold standard in mechanical heart valve prostheses.

"This generated tremendous excitement and put the Oregon Health Sciences University on the map," Starr said. "We had visitors from all over the world."



**Starr-Edwards cage-ball heart valve**

erated intense excitement and become established as the gold standard for mechanical heart valve prostheses. The valves maintained this status for many years, although today newer, low-profile valves are commonly used. There are, however, still some surgeons implanting the original Starr-Edwards cage-ball valve.



#### Human Valves Used in Other Humans

Not long after the first heart valves were implanted, physicians began searching for better heart valves — including biological valves. Biological valves are valves from animals or human cadavers or valves made from other animal tissue. An aortic **homograft** valve was first used in 1962 to replace a mitral valve in one pa-

tient and an aortic valve in another. Survival was short.

That same year, Dr. Donald Ross in England reported the first successful aortic valve homograft implant. He placed the valve in the normal position. A month later, Sir Brian Barratt-Boyes performed the same implantation in New Zealand.

Shortly after his success, Dr. Ross went on to develop another technique. In 1967, he used the patient's own pulmonary valve to replace a malfunctioning aortic valve. An aortic or pulmonary valve homograft was then used to replace the patient's pulmonary valve. This procedure, known as the Ross Procedure, is currently recommended for some younger patients who require aortic valve replacement.

#### Homograft:

A donor graft, or portion of tissue, taken from a donor and placed into a recipient of the same species.

Dr. Donald Ross was the first to successfully replace an aortic valve with a tissue valve from another human. He also invented the Ross Procedure, which is still in use today to replace a malfunctioning aortic valve.

## DONALD ROSS: THE VALVE PIONEER

**D**R. DONALD ROSS QUALIFIED for his medical degree on the same day as Dr. Christiaan Barnard, a fellow South African. Although the two would take divergent paths — Ross went to England to train and Barnard went to the United States — they remained friends, and both worked to develop heart transplantation. Ross recalled in an interview a conversation he had with Barnard before the first transplantation.

“Barnard came through one day and said, ‘I’ve just been watching Shumway do the trans-

plant of the heart in an animal and I’m going to do that,’” Ross remembered.

Later that same year, a reporter asked Ross when he thought the first heart transplantation would be performed. He predicted sometime within the next five years. Less than a month later, Barnard announced he had performed the first human-to-human transplant. Shortly afterward, Ross himself performed the first heart transplant in the United Kingdom.



Donald Ross

Although his work in heart transplantation was cutting edge, Ross became most famous for



Other tissues that have been used for valve implants include the pericardium, fascia lata, or tissue from tendons, and dura mater, which is the tissue that surrounds the brain and spinal cord.

In the 1960s, physicians also began to experiment with valves from other animals, or **xenografts**. This was first done in 1964 by Drs. Carlos Duran and Alfred Gunning in England, who replaced an aortic valve in a human by using a valve from a pig. The early results were good, but these valves often failed after a few years. In France, for instance, Dr. Alain Carpentier and his associates reported on twelve patients with pig valve replacements that all failed by five years. As a result, Carpentier developed a technique to fix the pig valves with a chemical called

glutaraldehyde instead of using the accepted formaldehyde. In addition, Carpentier mounted his valves on a stent, which allowed the valves to be used to replace the mitral and tricuspid valves.

Carpentier later wrote:

*"It became obvious that the future of tissue valves would depend on the development of methods of preparation capable of preventing inflammatory cell reaction and penetration into the tissue. My background in chemistry was obviously insufficient. I decided to abandon surgery for two days a week to follow the teaching program in chemistry at the Faculty of Sciences and prepare a Ph.D. (at the University of Paris). It was certainly not easy to become a student in chemistry*

**Xenograft:**

Graft tissue taken from an animal of one species and used in another species. Pig heart valves, which are commonly used to replace heart valves in humans, are one form of xenograft.

his pioneering work with heart valves. This was an area of interest from the beginning of his career. In July 1962, Ross implanted the world's first successful homograft valve (a tissue valve from a human cadaver) only two years after Starr and Harken implanted their heart valves. Ross recounted this historical implantation:

*"Lord Brock was my mentor and chief and put me onto repeating earlier pioneering work in homograft implantation [in the animal laboratory]. It was a very exciting time. We took human valves and human aortas and stored them by a process of freeze drying so they could keep for months.*

*"One day during surgery while I was scratching away at a calcified valve, the whole thing disintegrated and went down the sucker. We didn't have a valve and there were no valves in England. There were only Starr valves in America. So we took*

*one of those stored human valves, which was freeze dried, reconstituted it and sewed it in."*

Originally, the valve was supposed to be temporary until the surgical team could import a mechanical valve. The patient did well, however, and Ross switched to implanting homograft valves instead of artificial valves.

Over the next several years, he found that an aortic valve homograft worked well in the pulmonary valve position. That discovery led to an important milestone in valve surgery, the Ross Procedure. In this operation, the native pulmonary valve is relocated to the aortic position, and a homograft valve replaces the pulmonary valve.

It is a technically difficult operation that took almost two decades to gain widespread acceptance but it is performed today with excellent results. It has the powerful advantage that the new aortic valve will grow, an especially important quality for small children.

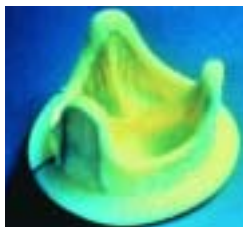


**Alain Carpentier**

Dr. Alain Carpentier (above) was a major figure in the development of pig valves for human hearts. His valves (below) were mounted on cloth rings to help physicians sew them in place.

#### **Cardiomyoplasty:**

A surgical procedure using a muscle, usually the latissimus dorsi muscle in the back, to wrap around a failing heart. The muscle is then electrically stimulated so it will contract in synchrony with the failing heart.



## ALAIN CARPENTIER

**D**R. ALAIN CARPENTIER DECIDED to go into medicine after an operation and a month-long stay in a hospital for appendicitis when he was only ten years old. At the time, antibiotics were not widely available, and his recovery was very long and painful, inspiring in the young boy a desire to help the course of healing. Today, he is best known for three major contributions to heart surgery. He developed surgical techniques to repair the mitral valve; he developed a practical method of using heart valves from pigs in humans; and he pioneered a surgical procedure called **cardiomyoplasty**, which is used in patients with failing heart muscle.

Carpentier began his research into heart valve replacement at a time when mechanical heart valves, such as the Starr-Edwards valve, had just recently become commercially avail-

able. Physicians were also successfully using heart valve implants from human cadavers, a technique pioneered by Ross and Barratt-Boyes. Inspired by their work, Carpentier began to research biological valve replacements but ran into a snag in French law.

“My surgical master, Dr. Charles DuBost, told me if I was interested, I would have to collect homograft valves, just like Barratt-Boyes and Ross did,” he remembered in a 1999 interview. “I began to try to collect homograft valves in Paris; however, French law did not permit one to take pieces from cadavers during the forty-eight hours following death to allow the family to make an opposition. Of course, after forty-eight hours, most of the homograft valves I could collect were infected.”

After a few months of this, Carpentier began researching the use of valves

*when you are thirty-five years old and an associate professor of surgery.*

*“I began to investigate numerous cross-linking-inducing factors and found that glutaraldehyde was able to almost eliminate inflammatory reaction.... My wife, Sophie, was a tremendous help all these years.”*

#### **Modern Heart Valve Therapy**

##### *Rheumatic Fever*

Today, surgeons are capable of treating a wide range of heart valve defects, which can be caused by a number of conditions. Rheumatic fever is a common cause of heart valve injury requiring surgery in adults. People of any age can contract rheumatic fever, but it's most

common in children between the ages of five years and fifteen years. It is caused by bacteria known as streptococcus and is usually related to a severe type of sore throat sometimes called a “strep throat.” Most people who have strep throats do not develop rheumatic fever, and appropriate treatment with antibiotics dramatically decreases the risk of developing rheumatic fever. Rheumatic fever usually occurs from two weeks to a month after the strep throat infection.

Symptoms of rheumatic fever include aches and pains in the joints. The pain in the joints tends to migrate from one joint to the next, and it's not always located in the same joint. Rashes can occur. Lumps, called subcutaneous nodules, can develop under the skin. Victims sometimes develop uncontrolled movements of the legs and

from other animals, or xenografts. It was this effort that led him to his work with glutaraldehyde and the technique to successfully replace any of the four heart valves with xenografts. He called these tissue heart valves, which were mounted on a cloth sewing ring, “bioprostheses,” a term that is still used today.

At the same time, he also developed what he considers his most important contribution to valve surgery: reconstruction of the mitral valve, as opposed to replacement of it. This question of valve replacement versus valve repair used to be answered during surgery. Today, Carpentier credits medical technology like echocardiography with greatly improving valve analysis.

“In the old days, I adopted a policy that I would try to repair the valve for fifteen minutes and if I was not satisfied after fifteen minutes, I would just replace the valve,” he said. “Progressively, the number of valves I had to replace di-

minished. Today, of course, is very different because we see patients at an earlier stage and we have the echocardiography technique, which I call the stethoscope of the next century because it is so useful.”

Valve repair was a superior option to replacement, according to Carpentier, because of the drawback of valve prostheses. “The reason I developed these two techniques almost simultaneously is the fact that, in 1966 to 1967, the only existing solution when a patient had a valvular problem was replacement with a mechanical valve,” Carpentier said. “I was struck by the fact that one of my patients was a painter and was obliged to stop his artistic activity after the operation. He was a well-known artist, and I found it a real tragedy that although the mechanical valve made it possible to save hundreds of lives, there was this problem of emboli (blood clots breaking away from the valve) and the need for anticoagulation.”

arms, called chorea. Patients with rheumatic fever can also develop an inflammation of the heart muscle called carditis, which can result in shortness of breath and fatigue. Fever can also be present.

Although it doesn't always do so, rheumatic fever can cause damage to any or all of the heart valves. The aortic and mitral valves are most commonly affected.

A second episode of rheumatic fever can further damage the heart, particularly the heart valves. Patients with damaged heart valves may need heart surgery relatively soon after their rheumatic fever. However, most people who need heart surgery will require it much later, sometimes late in life, even though they contracted rheumatic fever as a child. About half of all patients who require heart valve surgery as adults because of rheumatic

fever damage do not even know that they had rheumatic fever.

#### *Infectious Endocarditis*

Bacterial and fungal infections are another threat to both the heart and the heart valves (Fig. 10.5). In many cases, the exact reason for the infection is unknown. During a dental procedure, for example, bacteria may gain access to the bloodstream. Antibiotics should be given before a dental procedure to those who have a diseased or artificial heart valve to help prevent infectious **endocarditis**, or infection of the heart muscle. Other causes include surgery and illicit intravenous drug use.

In most cases, infections of the heart and heart valves can be treated with

**Endocarditis:**  
An infection inside the heart.

antibiotics. In some cases, however, one or more of the heart valves can be severely damaged by an infection and may require heart surgery to repair or replace the valve.

#### *Prolapsed Mitral Valve*

**Mitral valve prolapse**, or MVP, is a condition in which the leaflets of the mitral valve do not meet properly, usually because the chordae tendineae are too long (Fig. 10.2). Sometimes one or both valve leaflets are also abnormally enlarged. When the leaflets do not meet correctly, the heart valve may make an abnormal noise when it closes. This can be heard with a stethoscope. If they do not touch each other when they close, blood from the left ventricle can leak back into the left atrium. This can cause a heart murmur.

Some patients may have chest pain related to mitral valve prolapse. They may develop cardiac arrhythmias, or irregular heartbeats, and shortness of breath. Medications may alleviate these symptoms. Fortunately, the great majority of patients with mitral valve prolapse lead a normal life and do not need a surgical procedure. Some people with diagnosed mitral valve prolapse are also encouraged to undertake an antibiotic regime both before and after dental work, even teeth cleaning.

The cause of mitral valve prolapse is unknown. It is more common in women. Occasionally, patients require heart surgery, particularly if the chordae tendineae connecting the prolapsed mitral valve to the heart wall rupture.

#### **Aortic Valve Disease**

The aortic valve is responsible for regulating the flow of blood from the left ventricle into the aorta. As time goes by and the valve is subjected to stress, calcium may deposit on the leaflets and cause the valve to become stenotic, or constricted (Fig. 10.3). This process is accelerated by rheumatic fever. The leaflets (cusps) become scarred. Over time, the scar tissue increases, and the valve itself becomes calcified.

Aortic valve stenosis is also related to a condition known as a congenital bicuspid valve. In this condition, the aortic valve, which normally has three leaflets, has only two. The bileaflet valve does not usually cause problems in childhood, but after many years it tends to scar. As with rheumatic fever or stenosis, calcium builds up, and the valve orifice becomes very narrow. Bicuspid aortic valves tend to calcify in some people by age twenty years or thirty years. They

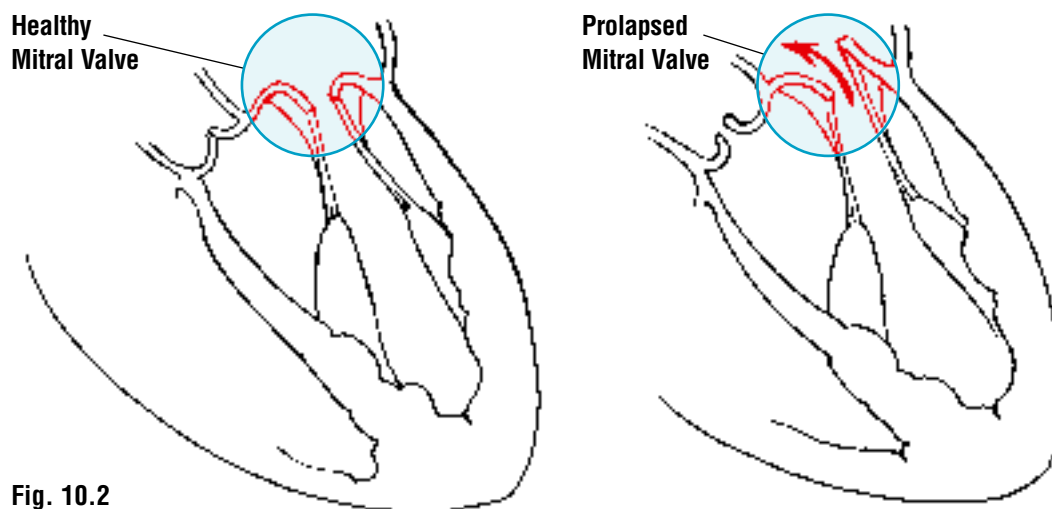


Fig. 10.2:  
**Mitral valve prolapse**, or MVP, occurs when the valve leaflets do not meet properly. The mitral valve on the near right is healthy. The mitral valve on the far right is prolapsed.

Fig. 10.2

usually become symptomatic between ages thirty years and sixty years.

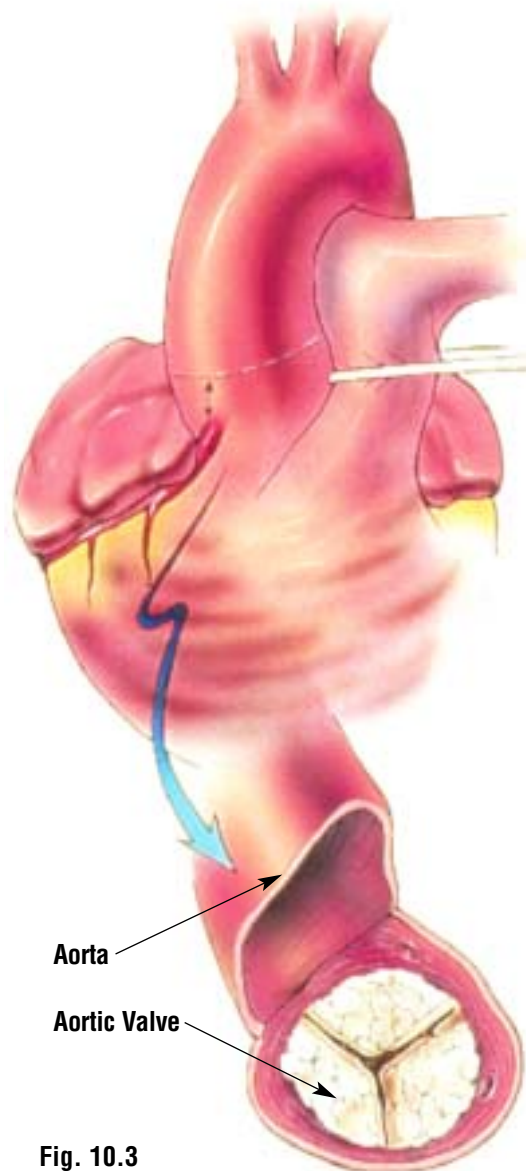
Stenotic aortic valves cause stress on the left ventricle, which is forced to work harder to push blood through the narrowed opening. As a result, the ventricular heart muscle will thicken, or hypertrophy, until it actually outgrows its blood supply. Finally, the left ventricle will no longer be able to force enough blood past the valve.

In this case, the heart itself may begin to fail, and patients usually start to develop symptoms including lightheadedness, or they may even pass out because not enough blood is getting to the brain. Irregular heartbeats and **angina pectoris** are also symptoms. This kind of angina occurs not only because the heart muscle outgrew its blood supply but also because not enough blood is getting past the narrowed aortic valve and into the coronary arteries that supply the heart.

Heart failure, signaled by shortness of breath and fatigue, is also associated with aortic valve stenosis. These symptoms are more commonly brought on by exercise, which increases the body's demand for oxygen. The severity of symptoms of aortic stenosis does not always correlate with the severity of the blockage. Sometimes the first sign of severe aortic stenosis is sudden death.

#### *Diagnosing Aortic Stenosis*

This condition can be diagnosed by using a number of different techniques. The first clue is frequently obtained with a stethoscope, which reveals a heart murmur that is rather typical of aortic stenosis. Further testing will be performed, including the two definitive tests that reveal aortic stenosis: echocardiography and cardiac catheterization. If the aortic stenosis is severe enough to warrant heart surgery, the patient will frequently undergo both tests.



**Fig. 10.3**

#### *Aortic Valve Incompetence*

Aortic valve incompetence, also called insufficiency or regurgitation, usually occurs when the three leaflets of the aortic valve do not come in contact with each other when the valve closes. Some of the blood that has just been pumped into the aorta leaks back into the left ventricle. This makes the left ventricle much less efficient because it pumps the same blood twice.

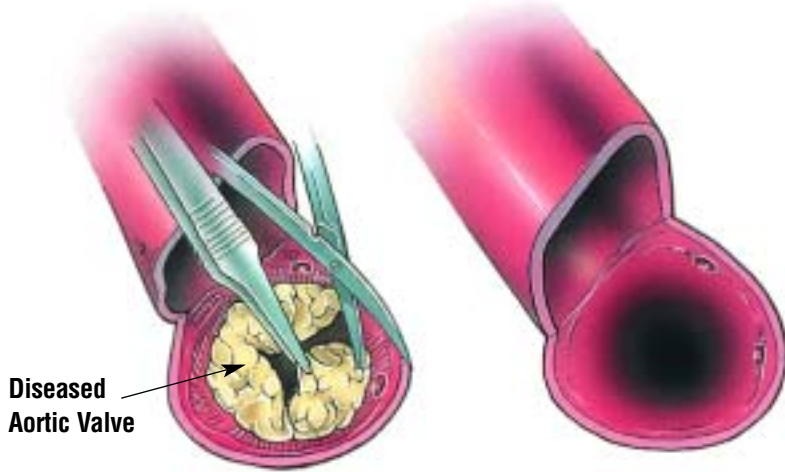
**Fig. 10.3:**

#### **Aortic Valve Stenosis:**

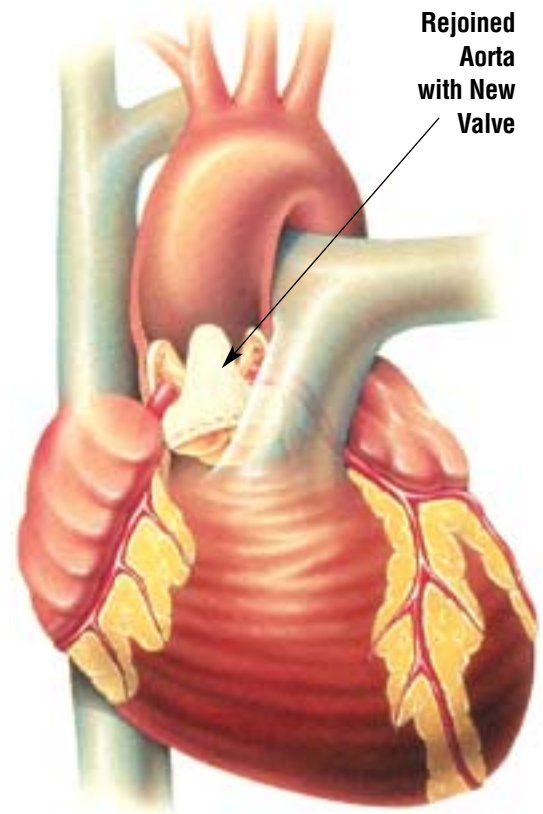
A condition in which the aortic valve is narrowed, which stresses the left ventricle because it has to work harder to get blood through the valve.

#### **Angina Pectoris:**

Chest pain that occurs when the heart is not getting enough blood. Often described as pressure, like a band tightening around the chest, or a dull, aching pain over the front left side of the chest. It can also be a pain radiating down the left arm or, occasionally, it can radiate into the neck or jaw.



**Diseased Aortic Valve**



**Rejoined Aorta with New Valve**

To correct aortic valve stenosis with a porcine valve, physicians remove the diseased aortic valve (above) and sew in a xenograft (below). The final illustration (above right) shows the aorta incision stitched closed.

Aortic valve incompetence can be caused by rheumatic fever (Fig. 10.4). It also can result from infective endocarditis or a number of other causes.

Aortic valve incompetence ranges in severity from mild to severe. Mild to moderate aortic valve incompetence is generally well tolerated. Most patients with mild or moderate aortic incompetence can lead a normal life and have a normal life expectancy. If the leakage becomes great, however, the left ventricle will start to dilate and fail. Patients can develop signs and symptoms of congestive heart failure, including shortness of breath and fatigue, and their ankles may become swollen. A definitive diagnosis is made with echocardiography and/or cardiac catheterization.

In some cases, aortic incompetence can appear rather quickly and be severe. This could be related to an infection in which one of the heart valve leaflets is destroyed, or it can happen as a result of trauma sustained in an automobile accident when the chest strikes the steering wheel. There can be other causes. In these situations, emergency heart surgery with heart valve replacement is necessary.

also be due to bicuspid aortic valve or aging. In either case, as the valve becomes deformed, narrowed, and stenotic, the leaflets no longer come together. Not only is the blood obstructed as it tries to leave the left ventricle, but when the left ventricle relaxes, some of the blood leaks back into the chamber. Heart valve surgery may be needed.

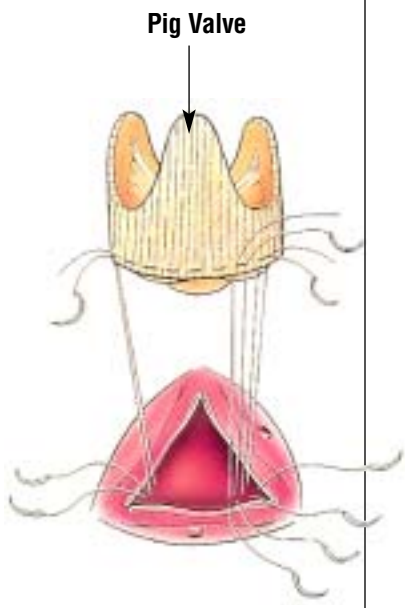
**Mitral Valve Disease**

*Mitral Stenosis*

Mitral valve stenosis is usually caused by rheumatic fever. In this condition, the two leaflets of the mitral valve gradually fuse together, making it difficult for the blood traveling into the left atrium from the lungs to pass through the mitral valve and into the left ventricle. As this condition becomes more severe, shortness of breath devel-

*Aortic Valve Stenosis and Incompetence*

A combination of aortic valve stenosis and incompetence is usually related to rheumatic heart valve disease but can



**Pig Valve**

ops because blood backs up into the lungs. Fatigue is also a common symptom. Also, some babies are born with an abnormally narrowed mitral valve

In some cases, the patient may cough up blood. (However, there are many other causes of coughing up blood [hemoptysis].) Depending on the degree of mitral valve stenosis, some form of intervention may be necessary. This might involve using a balloon catheter to dilate the stenotic mitral valve and could also mean heart surgery.

*Mitral Valve Incompetence*

Mitral valve incompetence, which is also referred to as mitral valve regurgitation or insufficiency, occurs when the two leaflets of the mitral valve no longer meet each other when the valve is closed. Because the leaflets do not meet, some of the blood that should be ejected into the aorta is squeezed through the faulty mitral

valve backwards into the left atrium as the left ventricle contracts. The resulting higher pressure in the left atrium sends blood backwards into the lungs.

This condition can cause shortness of breath and fatigue. The heart also has to work harder because some of the blood that's being pumped is going backwards. As a result, the left ventricle will dilate and begin to fail, adding to the shortness of breath. Patients also have swollen ankles. If this problem becomes severe, heart surgery will most likely be required.

Another condition is called **myxoid degeneration**, in which some of the tissues in the heart are weakened, and the valve is prone to incompetence. This condition can affect varying parts of the mitral valve. For example, the chordae, which attach the valve to the underlying muscles, can rupture (Fig. 10.4). Likewise, the papillary muscles can rupture. Papillary muscle rupture is usually related to a heart attack. This condition requires emergency heart surgery.

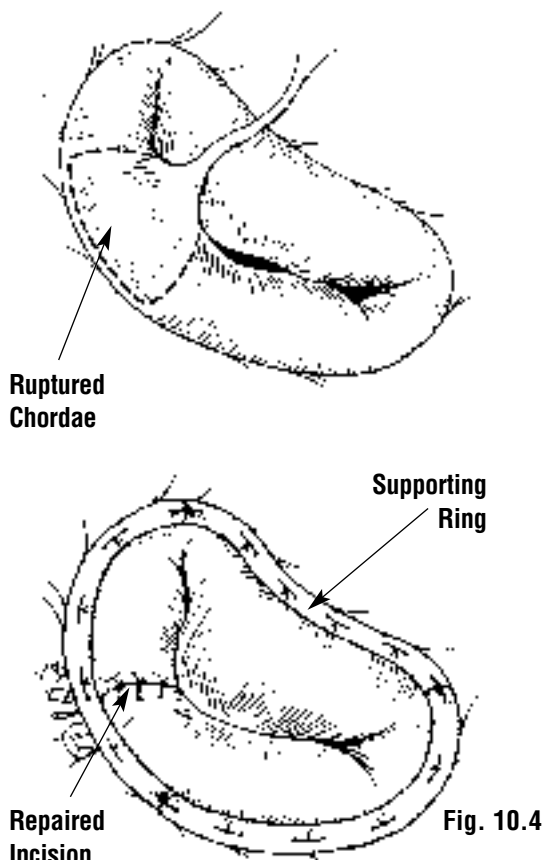
*Mitral Valve Stenosis and Incompetence*

As with the aortic valve, the mitral valve may deform so that it obstructs the flow of blood into the left ventricle and prevents it from closing normally because the two mitral leaflets no longer touch each other. In this condition, the valve is narrowed and incompetent, sending some of the blood back through the deformed valve. Depending on the severity of this problem, heart surgery may be required.

**Tricuspid Valve Disease**

*Tricuspid Valve Stenosis*

The tricuspid valve may become stenotic as a result of rheumatic fever, or it may be narrow at birth (Fig. 10.5). Tricuspid valve stenosis from rheumatic fever, particularly that which is severe enough



**Myxoid Degeneration:** Degeneration of the middle layer of tissue in blood vessels and heart valves.

**Fig. 10.4:** The mitral valve is attached to the ventricular wall by chordae. If these rupture, the mitral valve becomes incompetent. The surgeon removes that portion of the valve where the ruptured chordae is located (above), then sews the valve together and places a supporting ring (below).

to require heart surgery, is relatively uncommon.

If the valve is severely stenotic, blood returning from the veins to the heart will have difficulty getting into the right ventricle. As a result, the liver may become engorged, and fluid can build up in the abdomen. This fluid buildup is known as **ascites**. The legs and ankles may swell. If there's a small hole in the heart between the right and the left atrium, some unoxygenated blood may pass through this hole, and a patient may appear blue (cyanotic). Heart surgery may be required to correct this problem.

**Ascites:**

An abnormal accumulation of serum-like fluid in the abdomen.

the ring around the tricuspid valve that anchors the valve. This is commonly related to either long-standing mitral valve disease or pulmonary arterial and/or pulmonary venous hypertension, meaning the pressure in the pulmonary arteries and veins is elevated, forcing the right ventricle to work harder.

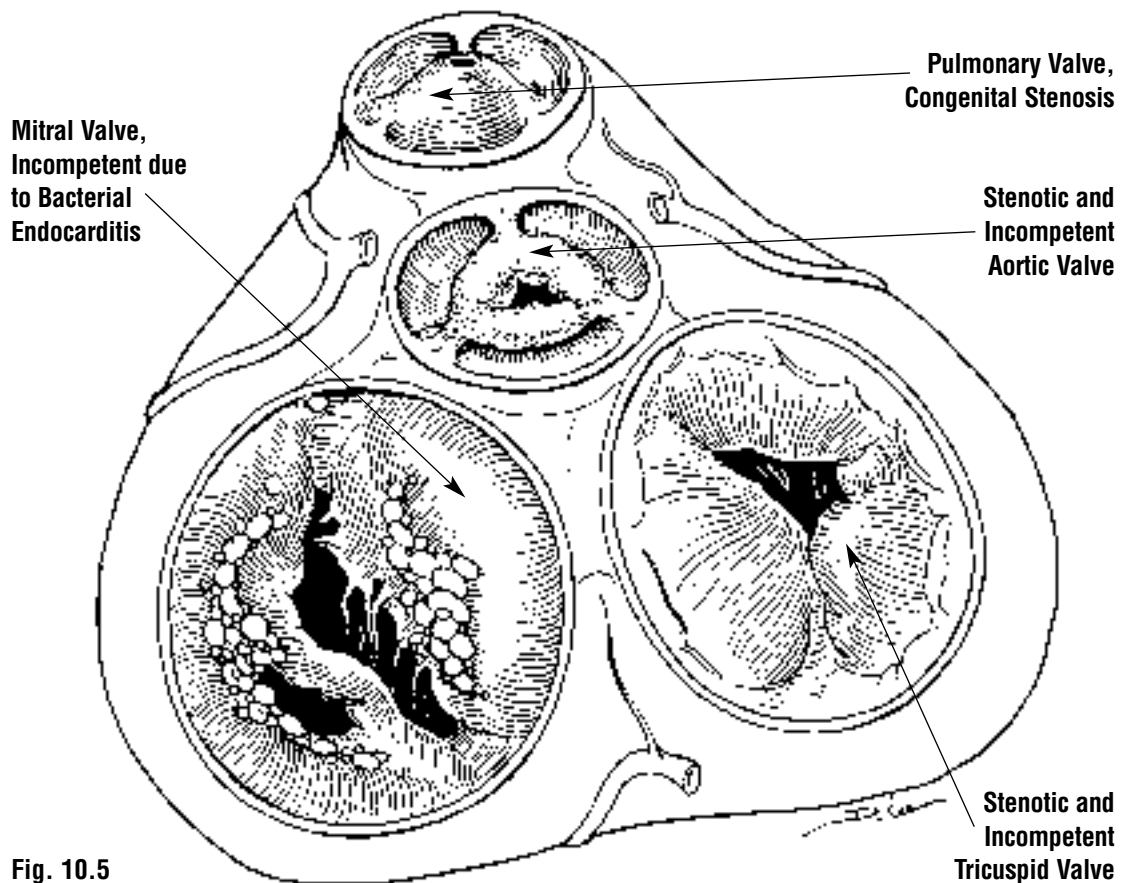
Over time, the right ventricle enlarges and begins to fail. As it does, the annulus may dilate and cause the tricuspid valve to leak blood back into the right atrium, causing similar signs and symptoms as in tricuspid valve stenosis (narrowed valve).

During an episode of endocarditis, bacteria or fungi can destroy the leaflets of the tricuspid valve. Depending on the severity of the condition, heart surgery may be required, and the valve may be repaired or replaced.

*Tricuspid Valve Incompetence*

Tricuspid valve incompetence is relatively common and usually related to dilatation of the tricuspid valve annulus, or

**Fig. 10.5:** This illustration shows four possible valve disorders. The pulmonary valve (top) suffers from congenital stenosis. The aortic valve (middle) suffers from stenosis and incompetence resulting from rheumatic fever. The tricuspid valve (far right) suffers from stenosis and incompetence. The mitral valve (near right) suffers from incompetence due to bacterial infection. The growths on the valve's surface are clumps of bacteria, and a hole has been eaten through the valve leaflet.



**Fig. 10.5**



Dr. Agustin Arbulu, a heart surgeon at Wayne State University in Detroit, has shown that when a tricuspid valve is severely damaged because of antibiotic-resistant infection and the infection is the result of illicit intravenous drug abuse, a good method of treatment is to remove the infected tricuspid valve and not replace it. This removes the source of the infection. If an artificial valve is put in, it too will likely become infected since the patient frequently resumes the illicit drug use.

#### *Tricuspid Valve Stenosis and Incompetence*

This combination is usually related to rheumatic heart disease, and the problem is similar to mitral and aortic valve incompetence/stenosis in which the valve is both leaky and narrow. Depending on its severity, this condition may require heart surgery.

### **Pulmonary Valve Disease**

#### *Pulmonary Valve Stenosis*

Pulmonary valve stenosis (narrowing) is most commonly of congenital origin in the United States (Fig. 10.5). Although it may occur as a result of rheumatic fever, this is relatively uncommon in the United States. Pulmonary valve stenosis can be treated with a balloon catheter, which is used to dilate the valve. Sometimes, however, heart valve surgery is needed.

#### *Pulmonary Valve Incompetence*

Pulmonary valve leakage (incompetence) is usually related to abnormally high pressure in the pulmonary arteries or pulmonary veins. This, in turn, may be due to a problem with the pulmonary blood vessels or with the aortic or mitral valves. In this case, the right ventricle may fail, causing the pulmonary valve annulus to dilate and

leak. The pulmonary artery may also dilate and cause the valve to leak. It is uncommon to need heart surgery for this condition.

The pulmonary valve may also become incompetent as a result of bacterial endocarditis. Sometimes, the valve may need to be replaced.

#### *Heart Valve Balloon Dilatation*

When heart valves, including the pulmonary valve, the mitral valve, or even the aortic valve, are narrow (stenotic), they can sometimes be dilated with a balloon. The balloon is attached to a catheter and inserted into the bloodstream through an artery or vein. After the catheter is placed within the narrowed heart valve, the balloon is inflated, which dilates the valve. If the valve is both stenotic and incompetent, however, physicians generally do not try to dilate the valve with the balloon catheter. Although the obstruction may be relieved to some degree, the valve would likely become more incompetent, thus trading one type of heart valve problem for another.

Mitral valves that are narrowed from rheumatic fever can sometimes be opened successfully with balloon catheters, similarly to the treatment of pulmonary valve stenosis. In fact, Dr. Zoltan Turi, a cardiologist at Wayne State University in Detroit, has shown in two randomized studies (published in the journal *Circulation* and *The New England Journal of Medicine*) that in certain patients, balloon catheter treatment for rheumatic mitral valve stenosis yields results that are as good as or better than surgery.

Balloon catheter therapy for congenital aortic valve stenosis can sometimes be life saving. This technique can buy time and delay heart valve surgery in some infants until they are in better condition to undergo elective heart valve surgery.

Balloon catheter therapy can also be used for rheumatic aortic stenosis or bicuspid aortic stenosis. However, the

longer-term results tend to be unsatisfactory. Aortic valve balloon catheter therapy is used in some adult patients who are desperately ill, perhaps even being treated with a mechanical ventilator. It is designed to improve their condition and decrease the risk of the aortic valve operation. It is also sometimes used in patients more than eighty years old who have numerous other serious medical problems, in hopes that their symptoms will improve, even though in most cases the improvement is short lived.

#### Heart Valve Surgery Repair versus Replacement

Most heart surgeons believe that if a heart valve can be repaired with the likelihood of relatively good long-term results, repair should be attempted rather than valve replacement. Although many excellent artificial heart valves are currently available, the perfect heart valve substitute has yet to be developed. If any one of the four valves is stenotic, physicians may be able to open the closed valve with a scalpel by carefully opening the fused leaflets, or commissures. This is called commissurotomy or **valvotomy** (Fig. 10.6). It is most commonly done in patients who require heart surgery for congenital pulmonary stenosis and those requiring mitral valve surgery for mitral valve stenosis related to rheumatic fever. The short-term and long-term results in both cases are quite good.

For mitral valve incompetence and tricuspid valve incompetence, there are numerous repair techniques that can be used depending on the circumstances.

#### Heart Valve Replacement

If the heart valve cannot be repaired, physicians will most likely recommend heart valve replacement with either a mechanical heart valve or a tissue (biological) heart valve.

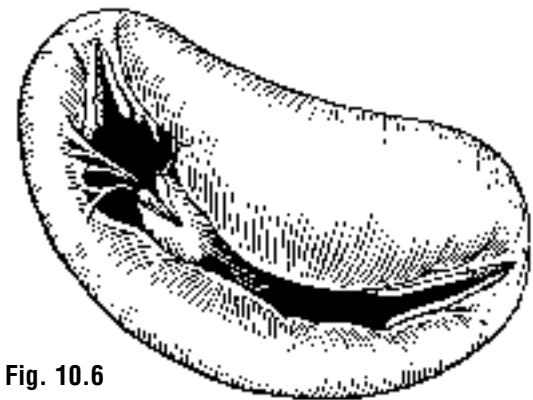
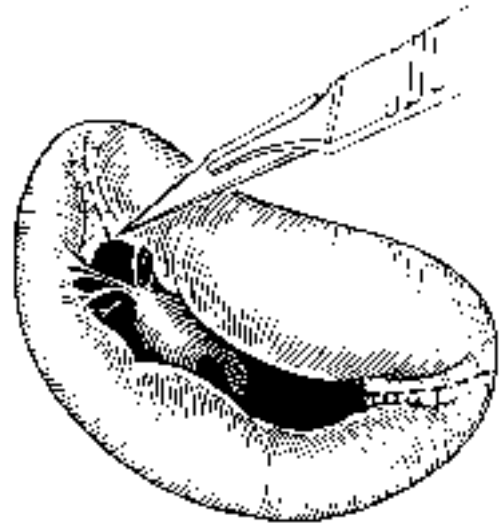


Fig. 10.6

When it comes to mechanical heart valves, some surgeons still use the original cage-ball valves. These valves have a good, long-term track record. Some patients have had the cage-ball valves for more than thirty years.

The newer mechanical heart valves are made from carbon. They tend to be low profile so they take up less space and have better flow characteristics. These types of valves have been put on pulse duplicators with which accelerated wear can be tested. Tests of one hundred simulated years of use show very little actual wear on the valve. These tests indicate that, in most cases, satisfactory function can be expected for many years.

**Fig. 10.6:** During a **valvotomy**, a surgeon can treat a narrowed valve by widening the valve with a scalpel (above). The corrected valve (below) will allow blood to move through more freely and therefore place less stress on the heart.

The biggest disadvantage of the mechanical heart valves is that most patients need to take an anticoagulant, also referred to as a “blood thinner,” to prevent blood clots from forming on the valve itself. The most common anticoagulant is coumadin, otherwise known as warfarin. Patients who take coumadin need to get their blood tested periodically. When coumadin treatment is first started, the blood is tested every day or two, but after a few weeks, it is usually tested every couple of months to make sure the level of anticoagulation is appropriate. If the anticoagulation is too great, the patient is more prone to develop bleeding problems, which can include bleeding into the stomach, intestines, brain, or kidneys. A person with bleeding ulcers would be prone to bleed more. If you were cut, you would have a problem with abnormal bleeding. The coumadin treatment can be reversed in an emergency situation if necessary.

Another problem related to mechanical heart valves is blood clots that occur even if the anticoagulation level is appropriate. These clots can form on or near the artificial valve and travel to various parts of the body, causing strokes and other problems. Fortunately, the incidence of this is small. It is somewhat more common in patients who have mechanical artificial heart valves than in those with tissue heart valves. The biggest advantage of



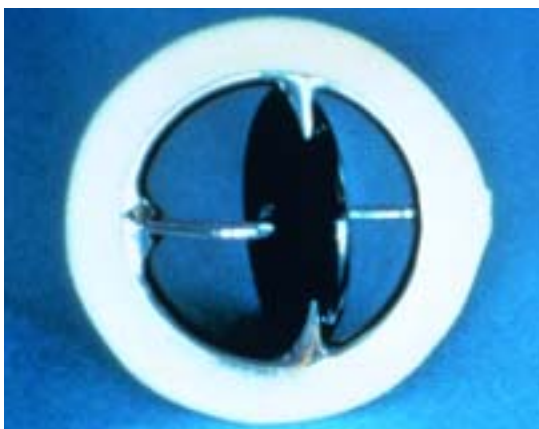
Above: A modern, bi-leaflet, low-profile heart valve made of carbon.

the mechanical valves is that the current models tend not to wear out.

Both mechanical and tissue heart valves are more prone to become infected than your own normal heart valves. Currently, the most commonly used tissue valves come from a pig. The pig valve can be used to replace any of the four human heart valves. Another type of tissue valve is made from the pericardium of a cow. The results with this valve seem comparable to those with the pig valve.

The problem with tissue valves is that they wear out, which occurs more rapidly in children and young adults. The degeneration of these tissue valves is slower in older adults, particularly those more than seventy years of age. In patients less than seventy years old, about 15 percent to 30 percent of the tissue valves wear out within ten years. The rate of valve deterioration increases greatly after the valves have been in place for ten years.

Another type of tissue valve is the aortic homograft valve, which is used to replace the aortic valve and sometimes the pulmonary valve. These valves come from a human donor and are removed right



Left: A tilting disc mechanical heart valve made by Medtronic.

A pig valve without a stent (inset) can be used to correct various abnormalities of the aortic valve.

after death. Like pig valves, they tend not to last as long in younger people and last longer in patients fifty years of age or older. The incidence of blood clot problems with these tissue valves is generally quite low. Most patients with tissue valves do not need to be anticoagulated.

Some patients who undergo aortic valve replacement have a procedure called the Ross Procedure. During this operation, patients have their own pulmonary

valve removed and used to replace the aortic valve. The pulmonary valve is then replaced with a human pulmonary or aortic valve homograft. This seems to be a particularly good operation for children, in whom the valve may grow with the child. Some groups have reported excellent results with this procedure, whereas others are less enthusiastic about it. Centers that have considerable experience with the Ross Procedure tend to have the best results.

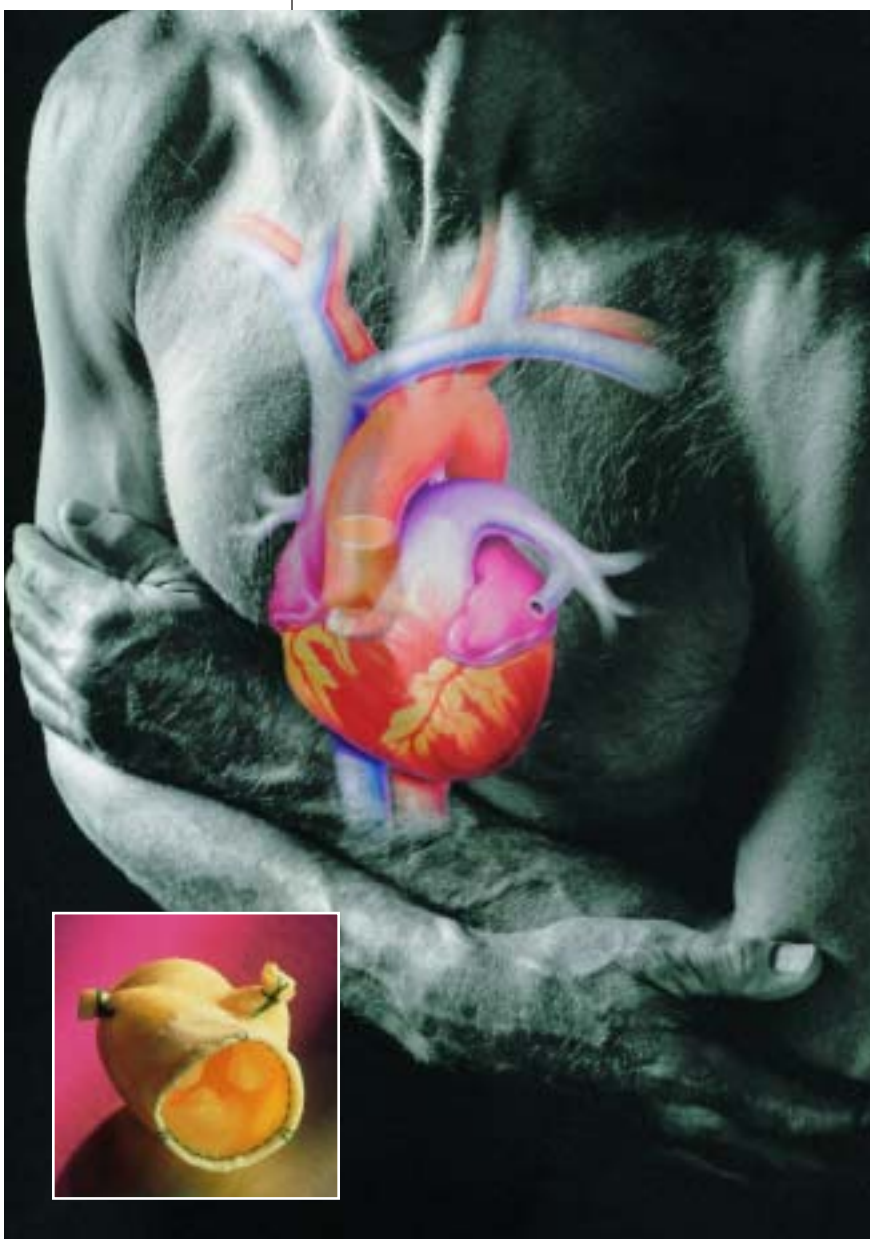
### The Heart Valve Operation

Many aspects of heart valve operations are similar to those of other forms of cardiac surgery. The patient is usually admitted to the hospital the morning of the operation. The procedure is performed after general anesthesia is induced. Operations are performed through a midline chest incision (from the base of the neck to the upper abdomen) through the breastbone, although some surgeons prefer to use other incisions depending on the circumstances.

The pericardium is opened, and the patient is connected to the heart-lung machine. The heart or a major blood vessel is opened, and the heart valve is repaired or replaced. After that, the heart or blood vessel is sutured closed, and the patient is disconnected from the heart-lung machine. The chest incisions are closed in layers with stitches, and the skin is closed with stitches or staples.

Afterward, the patient is transferred from the operating room to the intensive care unit (ICU). At this point, a mechanical respirator is breathing for him or her, and will for at least several hours. The patient is typically in the ICU for a day or two. Discharge from the hospital typically occurs from four days to nine days after the surgery.

When the patient returns home, he or she will be able to go out for walks. It will be about a month before driving a car is recommended. By then, many patients are



walking a mile or two a day. Some cardiologists feel that all of their patients should be enrolled in a cardiac rehabilitation program, whereas others feel that only more sedentary people need a formal rehabilitation program. Professional athletes might be able to resume normal strenuous activities, depending on a number of variables, about three months after heart surgery. Cardiologists determine when and what level of activity can be resumed and when it can be started after heart surgery.

The midline incision (through the breast bone) that is currently used for most valve replacement surgeries is not very painful for most people. Patients are usually discharged with a prescription for a relatively mild pain medicine.

So how many heart valves can be replaced in the same person? The aortic valve is the most commonly replaced. The second most commonly replaced is the mitral valve. Third is replacement of both the aortic and mitral valves during the

same operation. Sometimes the aortic, mitral, and tricuspid valves are all replaced at the same time. More typically, the aortic and mitral valves are replaced, and the tricuspid valve is repaired. This treatment is usually reserved for long-standing aortic and mitral valve disease in which the tricuspid valve has become incompetent as a result of the other two valves causing stress on the right ventricle and tricuspid valve. Occasionally, the mitral and tricuspid valves are both replaced. Rarely, the aortic and tricuspid valves are replaced at the same time.

I am aware of one patient, a young girl, who had stenosis of all four valves related to rheumatic fever. All four valves were opened at surgery with a commissurotomy procedure. She was alive and well one year later. I am also aware of one patient who underwent replacement of all four valves. This was at the Mayo Clinic. The patient survived for about six months and then died of unrelated complications.

# ROBOTIC HEART VALVE SURGERY: IS THIS REALITY OR MYTH?

By

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**I**N THE LAST SEVERAL years, the public has become entranced by the idea of reducing both the psychological and the physical effects of heart surgery. Minimally invasive techniques have recently emerged as one way to speed patient recovery, reduce discomfort, and reduce the economic impact of these expensive operations. Unfortunately, despite rapid, multiple advances in other surgical specialties and interventional cardiology, heart surgery has lagged behind in the development of less invasive methods.

Cardiac surgeons have been afraid of accepting the added risk of performing major heart operations through tiny incisions and obtaining less-than-excellent results. In fact, our surgical teachers, many of whom are featured in this book, taught that exposure of the entire heart and great vessels was central to performing safe, technically excellent surgery.

In the early 1960s, it was a feat to have patients survive even simple heart valve operations.



Most patients were at the end stages of their cardiac disease, the heart-lung machines were crude, and heart valve prostheses were in early evolution. Moreover, these were uncharted waters for surgeons regarding technique and postoperative care. In spite of these impediments, pioneers in heart surgery took the necessary first steps.

Years later, minimally invasive cardiac surgery is emerging with no less skepticism and criticism. However, simultaneous near-meteoric advances have been

made in both Europe and the United States. After just three years, we are beginning to see improvements in our specialty and what may be a renaissance in cardiac care. Evolving technology has afforded us opportunities to make these changes safely.

Many of us think it is time to make bold steps in cardiac care. Advances in heart-lung perfusion, surgical mini-cameras (endoscopes), “smart” instruments and robotics, and cardiac cellular protection have catapulted us to a better position. Moreover, standard heart operations are safer than ever. For example, both coronary bypass and heart valve operations in uncomplicated cases can be performed with only a 1 percent to 2 percent operative mortality, even in the elderly.

Why should we try to improve on these outstanding results? Technology has allowed some surgeons to envision ways to improve heart operations. Still, most heart surgeons perform operations through large breastbone incisions. Patient recovery is slow

because of muscular and skeletal tissue trauma rather than the operation on the heart itself. Thus, surgeons are now asking themselves: Can quality coronary bypass and valve operations be done through tiny access ports using endoscopes and miniaturized instruments, and even robotic assistance?

### **Minimally Invasive Valve Surgery — The Beginnings**

The trek to a completely closed chest heart operation may be compared to a Mt. Everest ascent. There are multiple levels of accomplishment established before reaching the summit. This surgical trek began at a “base camp” that was the conventional valve operation with a breastbone incision. All new procedures are being compared to this gold standard.

Although widespread adoption has been slow, many cardiac surgeons already have learned to use less invasive techniques to replace and repair valves and place coronary artery grafts. They can do this safely, with demonstrated expertise and improved outcomes.

The first minimally invasive valve operations were done in 1996 through smaller incisions yet under direct vision. Clinical results in the last three years have been excellent. Dr. Delos Cosgrove of the Cleveland Clinic Foundation and Dr. Lawrence Cohn of Brigham and Women’s Hospital pioneered much of this early work.

Operative results have been excellent in hundreds of patients who had both aortic and mitral valves repaired and replaced through smaller chest incisions

(four to five inches) with a 1 percent operative mortality.

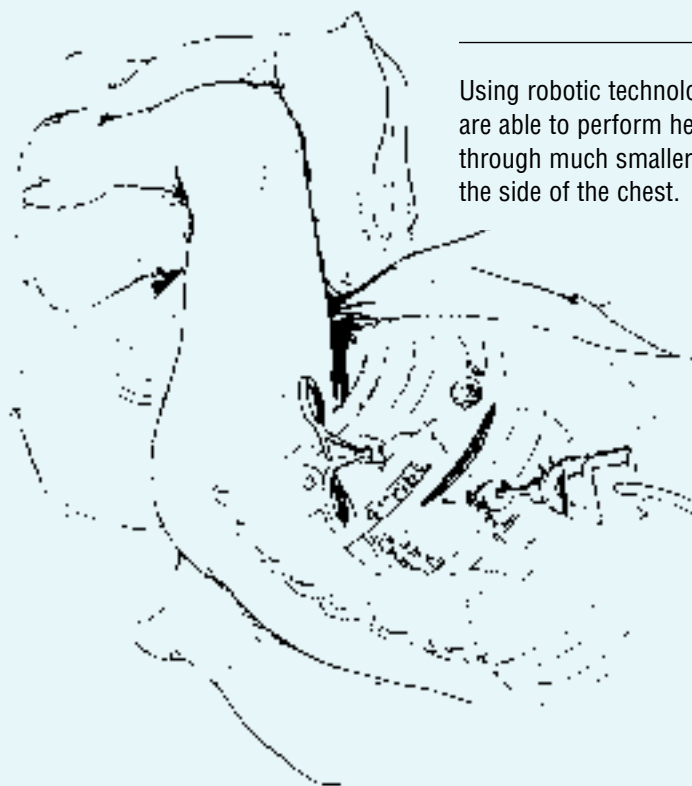
Others have followed and shown that these results can be reproduced in many local hospitals. Using more expensive aortic balloon occlusion devices, namely the Port-Access™ device (Heartport, Inc., Redwood City, California), the Stanford University and New York University groups have operated through even smaller chest incisions (3 inches to 3.5 inches) to repair and replace mitral valves effectively with a 2 percent mortality.

### **Video-Assisted Minimally Invasive Mitral Valve Surgery: Trekking to Robotic Heart Surgery**

Once these valve operations, performed under direct vision through a smaller incision, were accomplished, the door was

opened to the use of tiny cameras for secondary vision. This allowed surgeons to operate through even smaller incisions. Ultimately and hopefully, physicians will be able to perform true closed-chest cardiac surgery by using a monitor or head-mounted visual display to see the inside of the chest. The use of computer-assistance and robotic techniques may one day allow a completely endoscopic heart valve operation. These devices continue to evolve at a very rapid pace.

Dr. Alain Carpentier in Paris performed the first video-assisted mitral valve operation in February 1996. Three months later, our group at East Carolina University performed the first videoscopic mitral valve replacement in North America. Since then, more than ninety minimally invasive video-assisted mitral valve replace-



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Using robotic technology, surgeons are able to perform heart operations through much smaller incisions in the side of the chest.

ments or repairs have been done at our center. Details of the results in the first thirty-one patients were published, as was the technique.

To perform these operations, an even smaller (2.5-inch) chest incision was used, and intracardiac instrument manipulation was performed using videoscopic vision. There were no operative deaths, and midterm results were excellent. Both transfusion and ICU requirements were markedly less than with the breastbone incision, and the length of stay averaged 3.5 days. There have been few major complications. Each videoscopic operation is now performed with an effort similar to that in a conventional operation. Overseas doctors have also pioneered videoscopic mitral valve surgery, working through tiny, two-inch incisions, and have had excellent results in more than two hundred patients.

#### Robotics: The Final Ascent

Surgeons and patients reviewing this emerging area of heart surgery will have to judge whether widespread, truly endoscopic or even robotic (computer-assisted) valve operations are possible. In the past, three-dimensional vision was not possible unless the surgeon viewed the operation with his or her eyes. Recently, however, new video devices have been developed that are very

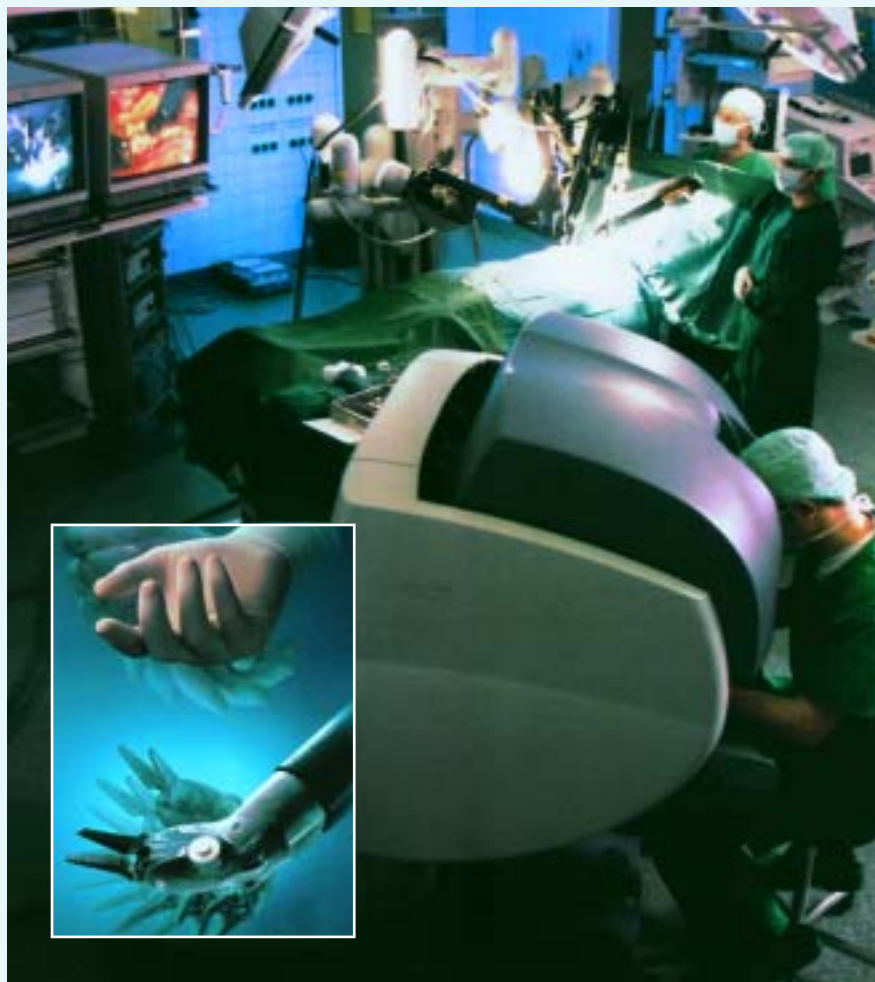
promising. Using both three-dimensional Zeiss™ and Vista™ systems, doctors in Germany, as well as our group, have performed “video-directed,” or completely endoscopic, mitral valve replacements.

Each surgeon worked with either a head-mounted display or a television monitor. Currently, three-dimensional intracardiac cameras are somewhat large (10 to 15 mm); however these are evolving rapidly toward the 5-mm size. These three-dimensional devices give us a look inside the heart as never seen before — the small papillary muscles look like trees, the fine chords to the valve

now appear as ropes, and the valve itself looks like a parachute rather than a small (about 1.5-inch) potato-chip-like structure.

Many of us have worked with evolving robotic methods. Early costs have been great and video-dexterity expertise difficult to develop. However, it is clear that new technology will allow voice-activated camera manipulation, scaling and tremor elimination of instrument motion, camera tracking of the operative field, flexible intracardiac articulation of small instrument tips, and three-dimensional vision.

During computer-assisted or robotic cardiac surgery, the



The robotic operating room at the Leipzig Heart Center in Germany. Inset: The wrist-like robotic instrument is capable of intricate movement.



surgeon moves the instrument within the chest by manipulating instrument-like electronic sensors. The robotic unit requires a “master” and a “slave” unit. The surgeon sits at a master console located a distance from the patient, and the slave unit is within the patient’s chest. The physician’s hand and wrist motions are translated directly to the robotic instruments, which are inserted through the chest wall.

There are two effector components common to all surgical robotic systems. Advanced computer technology has enabled direct translation of electronic data from the master console into fine mechanical motion in the slave unit. The camera tracks the operative site, and instrument tips are controlled by complex sliding internal cables within mechanical arms.

Unfortunately, complex instruments can be made only so small and still function well. Moreover, mechanical limitations and chest anatomic variations have caused intrathoracic instrument conflicts (much like sword fighting). Despite these limitations, massive progress in robotic cardiac surgery has been made in the last two years. To date, we have done thirty mitral operations using the Aesop™ (Computer Motion, Inc., Santa Barbara, California) voice-activated camera-directing robot. This device has made the operation easier for surgeons and reduced operative time but has not decreased costs or improved

operative quality. However, it has provided the first step in robotic cardiac surgery.

On May 21, 1998, Carpentier and Dr. Didier Loulmet at Broussais Hospital in Paris successfully performed the world’s first truly robotic-assisted heart operations in mitral valve patients. In these cases, intracardiac “wrist” instruments were manipulated from outside the chest. The surgeon, sitting at a master console, “drove” the instrument in the heart using the slave robot. This device provides true telemanipulation of a variety of coronary and valve instruments within the chest.

One week later, Dr. Friedrich-Wilhelm Mohr’s group in Leipzig successfully performed five mitral repairs using the same system. This latter group has performed more than twenty mitral repairs totally endoscopically using a DaVinci™ device (Intuitive Surgical, Inc., Mountain View, California).

Recently, I had the opportunity to be the first American to perform a true robotic mitral valve repair while working in Leipzig with Mohr’s group. The operative facility and translated hand movements with this device are superb; however, other challenges surely await us. The Leipzig group has brought the field of robotic coronary and valve surgery from fantasy to reality and to the forefront.

Other groups in France, Belgium, and Germany are beginning to apply this device to cardiac operations. To date, both the DaVinci™ and Zeus™ surgical

robots await FDA approval in the United States. Early results using these true robots appear to parallel those of both prior videoscopic operations and of conventional mitral valve operations.

Thus, within the last three years, cardiac minimally invasive surgery has developed from a concept to a working application. The current enthusiasm of surgeons worldwide, combined with rapid technological development and communications, appears to be moving us toward even less traumatic and maybe “microinvasive” cardiac operations. Yes, the spirit of innovation for better patient care is in the air! Yet many techniques are evolving so rapidly that large multipatient series have not been done. However, data from series of patients are beginning to be collected, and analysis of these data should be enlightening.

Surgeons always will ask themselves: Is this new method really offering our patients reduced trauma, fewer complications, more rapid recovery, and better long-term results, compared with traditional operations? A healthy mix of scientific skepticism and wisdom must be exercised. The public must ask penetrating questions regarding efficacy and outcomes. Yes — some of us believe that microinvasive reconstructive cardiac surgery will be a reality, and robotic cardiac surgery will probably be a reality rather than a fantasy. But the trek up Mt. Everest is not over — we have just arrived at a new base camp.

# MINIMALLY INVASIVE HEART VALVE SURGERY

By

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and

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**T**HOUSANDS OF PEOPLE benefit from heart valve repair or replacement every year. Heart valves require surgical correction when they become narrowed (stenotic) or when they begin to leak (become regurgitant). Although there are four heart valves, surgery is most often necessary for diseases of the mitral valve and the aortic valve. When these two valves become severely dysfunctional and cause symptoms, valve repair or replacement is indicated; there are no effective non-surgical treatments.

Traditionally, during heart valve surgery with the heart-lung machine, the heart was approached through a long incision down the middle of the chest. The breastbone, or sternum, was split in two, allowing access to the entire heart and the great vessels. This incision is called a median sternotomy. Recently, however, it has become apparent that heart valve surgery can be accomplished through a far smaller incision.



**Delos M. Cosgrove, M.D.**



**A. Marc Gillinov, M.D.**

When a patient needs valvular heart surgery and does not require a coronary artery bypass graft, a variety of smaller incisions allow the mitral and aortic valves to be seen. These incisions generally fall into two categories: thoracotomy, or an incision in the side of the chest between the ribs, and partial sternotomy, or an incision in the middle of the chest that divides only a portion of the sternum. Using these smaller incisions to accomplish heart valve surgery is called minimally invasive heart valve surgery. At the Cleveland Clinic Foundation, heart valve surgery is performed through a 2.5-inch to 3.5-inch skin incision and a partial upper sternotomy. A large portion of the sternum is left intact, decreasing postoperative pain and hastening healing.

Since 1996, we have performed more than one thousand heart valve operations using this incision. The average patient age was fifty-six years, and the oldest patient was eighty-four years old. More than six hundred

## MINIMALLY INVASIVE HEART VALVE SURGERY

patients had mitral valve surgery, and nearly 90 percent of these patients had mitral valve repair. Three hundred patients had aortic valve procedures, including valve replacements with a variety of artificial valves and a considerable number of aortic valve repairs.

Overall, operative mortality was less than 1 percent, and wound infections occurred in only 0.3 percent of patients.

The average length of stay in intensive care was one day, and the average hospital stay was six days.

These results demonstrate that minimally invasive heart valve surgery can be performed very safely with a low risk of complications. There are many advantages to minimally invasive heart valve surgery. There is less blood loss, and patients generally report less postoperative discomfort.

Less time is spent in the intensive care unit and in the hospital, and recovery at home tends to be rapid.

The next decade is likely to bring even more ingenious approaches, including robotically assisted cardiac valve surgery. These advances promise refinements to minimally invasive heart valve surgery, further reducing hospital stays and increasing patient satisfaction.

# TISSUE ENGINEERING OF CARDIAC VALVES AND ARTERIES

By

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**T**ISSUE ENGINEERING unites engineering and biology in an attempt to develop replacement tissues. Normal tissues draw much of their strength and flexibility from specialized proteins and polysaccharide-protein complexes that are produced by their cells. Although it has been possible to grow specific types of cells in the lab for some time, it is difficult to cause these cells to organize into the complex structures that are found in normal tissues or to produce normal structural proteins in an organized fashion.

To overcome this challenge, we are attempting to "grow" heart valves and large arteries by using biodegradable polymers as temporary scaffolds. These polymer scaffolds provide the structure and stability necessary for tissues to develop. Ideally, these scaffolds would degrade as the cells produce normal structural proteins and begin to replicate normal, organized tissue structures.



Diseases of the heart valves and large arteries account for about sixty thousand surgeries each year in the United States, including many replacement surgeries with synthetic substitutes. Ideally, any valve or artery substitute would function like the normal valve or artery, allowing blood to pass through it without narrowing or leakage, but it would also have the following characteristics: 1) durability, 2) growth potential, 3) compatibility with blood so that blood clots will

not form on its surface, and 4) resistance to infection.

None of the currently available devices constructed from prosthetic or biological materials meets these criteria. Our concept, however, was to develop new valves or arteries from individual cells in the hope that these new tissues will have these desirable characteristics. The potential for growth is of particular importance to children with malformed or diseased valves or arteries.

Several projects have been undertaken in our laboratory to construct a heart valve leaflet and large arteries by using tissue engineering. We used cells from normal arteries that could be removed and separated into the various cell components. We found it was important to use the animal's own tissue as the source of the cells, thereby eliminating the possibility of immune rejection once the tissues were reimplanted. The cells were "expanded" in cultures by allowing them to divide, and then suspen-

sions of the cells were mixed with the polymer scaffolds. The cell-polymer constructs were then incubated in culture for several more days before they were implanted as a valve replacement or an artery replacement. Valve leaflets and segments of large arteries functioned well for up to four months without structural failure or formation of blood clots on their surfaces. Importantly, when these structures were implanted into growing animals, they demonstrated growth. The tissues appeared to have relatively normal structure, and they produced the normal matrix proteins.

Despite these encouraging results, many questions remain to be resolved.

- ♥ First, all of these experiments have been carried out in animals, and it remains to be determined if human cells could be used to develop tissues in the same way.
- ♥ Second, the polymer used as the scaffold in these initial experiments is stiff, biodegradable polymer that may or may not have acceptable strength and flexibility (“handling”) characteristics while still providing a hospitable environ-

ment for the cells to develop into tissues.

- ♥ Third, the ideal source of the cells for the developing “tissues” has not been determined. In patients, it would be preferable to use veins rather than arteries as the initial source of the cells because veins are more plentiful and their removal does not compromise blood supply to normal tissues. We have some evidence that heart valves developed by using cells from the skin do not function as well as those developed with cells from the wall of the artery, but vein wall cells seem to work reasonably well.
- ♥ Fourth, because all of our experiments have been carried out in immature growing animals, it is not clear whether the cells that are used to form these “tissues” must be from immature animals. There is some reason to believe that fetal cells would be preferable. Because it is now possible to diagnose many forms of congenital heart disease while the embryo is still in utero, one might imagine using fetal cells to develop replacement valves or ar-

teries while gestation is continuing. At birth, these replacement valves or arteries could be ready to be implanted.

- ♥ Fifth, it is not clear whether the “tissues” should be implanted while they are still dependent on the polymer scaffold for their physical integrity or if they should be allowed to develop further in culture before implantation into the body. One of our current ideas is that if the developing tissues are subjected to physical forces and/or chemical signals while in the laboratory, it may be possible to guide their development further before implantation into the body. Our understanding of how these developing tissues will respond to any number of physical and chemical signals remains very limited.

Tissue engineering is one new approach to solving the problem of creating replacement tissues for use as heart valves or arteries. Although initial animal studies have been encouraging, numerous questions must be resolved before we embark on clinical trials in humans.

# DIET PILLS AND HEART VALVE PROBLEMS

By  
Larry Stephenson, M.D.

ON OCTOBER 8, 1999, AN article appeared on the front page of *The New York Times* with the headline, "Fen-Phen Maker to Pay Billions in Settlement of Diet-Injury Cases." This article is hopefully the final chapter in the story of the popular diet drugs, which were removed from the market after they were linked to heart valve problems. According to *The New York Times*, anybody with a pill-related heart valve injury could receive as much as \$1.5 million.

*"Some six million people took the diet drugs, Pondimin, American Home Products brand name for fenfluramine, the 'fen' in Fen-Phen, and Redux, a similar drug.*

*"The drugs were hailed earlier in the decade as miracle pills for obesity, as an alternative to pure diet and exercise. Diet centers actively promoted the pills to the obese and even to people who wanted to lose a few pounds. In 1996, doctors wrote*



*eighteen million prescriptions for the two drugs.*

*"But in September 1997, the company removed the drugs from the market at the request of the Food and Drug Administration after studies linked them to heart valve damage."*

What is the specific problem caused by these drugs?

In the August 28, 1997, issue of *The New England Journal of Medicine*, a group of doctors from the Mayo Clinic reported on twenty-four women who had taken

Fen-Phen and had no previous history of heart disease. These women were evaluated at an average of one year after their initial treatment with Fen-Phen. All had leaky heart valves. Two required surgical repair of their mitral valves, two, replacement of their mitral valves, and one patient, replacement of her aortic valve and mitral valve and repair of her tricuspid valve.

In their report, the doctors from the Mayo Clinic concluded, "These cases arouse concern that therapy may be associated with valvular heart disease. Candidates for fenfluramine-phenteramine therapy should be informed about serious potential adverse effects, including pulmonary hypertension and valvular heart disease."

The following year, another article appeared in *The New England Journal of Medicine* by a group of doctors from Minneapolis who had studied more than two hundred patients who had received Fen-Phen therapy compared with a

group who had not. They found that a greater percentage of the patients receiving Fen-Phen had cardiac valve abnormalities than those who had not taken the drug.

In the same issue of *The New England Journal of Medicine*, a group of doctors from Georgetown University in Washington, D.C., reported on a study of patients taking dexfenfluramine (a related drug) in which they found a small increase in the prevalence of aortic and mitral valve leakage.

Over the next year, twelve additional articles and letters to the editors appeared in *The New England Journal of Medicine* dealing with a possible link between appetite suppressants and valvular heart disease as well as a relation between high blood pressure in the pulmonary arteries and these drugs. There was considerable controversy among these doctors as to what the chances were of developing heart valve disease problems after Fen-Phen therapy.

Perhaps Dr. Richard B. Devereux from New York Hospital-

Cornell Medical Center summed it up best by stating:

*“What advice should we offer patients based on these findings?”*

*“First, all patients who receive fenfluramine or dexfenfluramine should be examined clinically. Echocardiography should be recommended for those who have a heart murmur or other evidence of valvular disease, as well as those who received one of the drugs for three or more months or at high doses....”*

*“Second, standard prophylaxis against endocarditis (heart infections) should be recommended to patients with a heart murmur, those with ‘silent’ moderate or severe regurgitation ... and those with mild regurgitation....”*

*“Third, in view of the delay in recognizing the association between the use of appetite suppressants and cardiac-valve abnormalities, caution should be urged in the long-term use of other agents that act on serotonergic mechanisms, albeit by different*

*pathways [meaning drugs that have similarities in the way they work].*

*“Finally, it is important to remember that in patients who meet the FDA criteria for cardiac-valve abnormalities on echocardiography performed soon after the discontinuation of appetite suppressants, there is a possibility (ranging from as low as 5 percent to as high as 67 percent) that the abnormality is a naturally occurring phenomenon and not a consequence of drug use.”*

The bottom line is, anyone who has taken these drugs should be checked by their doctor for symptoms of heart valve disease and/or pulmonary artery hypertension. If symptoms are present, a cardiologist will do a further evaluation.

The good news at this point is that the majority of patients who have taken these drugs seem to be doing quite well and have trivial, if any, heart problems.