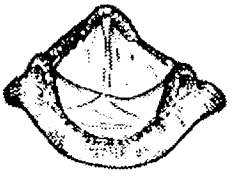
Edwards Lifesciences

Carpentier-Edwards S.A.V. Bioprosthesis Model 2650



Instructions for Use

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.

1. DEVICE DESCRIPTION

The Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 is a trileaflet stent-supported bioprosthetic valve comprised of porcine aortic valve tissue mounted on a flexible frame. The bioprosthesis is processed with the XenoLogiX Treatment, which uses ethanol and polysorbate-80 (a surfactant), and is packaged and terminally sterilized in glutaraldehyde. Glutaraldehyde is shown to both reduce the antigenicity of tissue xenograft valves and increase tissue stability; however, glutaraldehyde alone has not been shown to affect or reduce the calcification rate of the valve. The preservation or "fixation" of the valve is performed under 0 to 4 mmHg pressure to minimize alterations in the collagen waveform of the aortic valve tissue.

The Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 is designed for supraannular placement in the aortic position. The valve is available in mounting diameter sizes, 21, 23, 25, and 27 mm.

The flexible frame or wireform of the valve is composed of Elgiloy and is covered with a polytetrafluoroethylene (PTFE) cloth. It is designed to be compliant at the orifice and commissures to reduce the closing loading shocks at the commissures and free margin of the leaflets.

A polyester film band surrounds the base of the wireform frame. A suture ring covered with PTFE cloth is attached to the wireform frame. The suture ring contains inserts of silicone rubber and non-woven polyester. Two parallel marking sutures are located on the suture ring to denote the smallest intercommissural distance and are intended to aid in the proper orientation of the prosthesis.

2. INDICATIONS FOR USE

The Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 is indicated for patients who require replacement of their native or prosthetic aortic valve.

3. CONTRAINDICATIONS

None known.

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4. WARNINGS
FOR SINGLE USE ONLY.

DO NOT RESTERILIZE THE VALVE BY ANY METHOD. Exposure of the bioprosthesis or container to irradiation, steam, ethylene oxide, or other chemical sterilants will render the bioprosthesis unfit for use.

DO NOT FREEZE OR EXPOSE THE VALVE TO EXTREME HEAT. Each bioprosthesis in its jar is shipped in a molded foam enclosure containing a temperature indicator, which is intended for monitoring the temperature that the device is exposed to during transit. If the indicator has been activated, indicating the valve has been exposed to freezing temperatures or has had prolonged exposure to heat, do not use the valve. Please refer to the Storage section (10.2) for further instructions.

WARNING: Accelerated deterioration due to calcific degeneration of the bioprosthesis may occur in:
- children, adolescents, or young adults;
- patients with abnormal calcium metabolism (e.g., chronic renal failure, hyperparathyroidism).

DO NOT USE the bioprosthesis if the tamper evident seal is broken.

DO NOT USE the bioprosthesis if the container is leaking, damaged, or the glutaraldehyde solution does not completely cover the bioprosthesis.

DO NOT EXPOSE the valve to any solutions, chemicals, antibiotics, etc., except for the storage solution or sterile physiological saline solution, as irreparable damage to the leaflet tissue may result that is not apparent under visual inspection.

DO NOT ALLOW the valve tissue to dry. It must be kept moist at all times. Maintain tissue moisture with sterile physiological saline irrigation on both sides of the leaflet tissue.

DO NOT PASS CATHETERS, transvenous pacing leads, or any surgical instrument across the valve since it may cause tissue damage.

DO NOT USE the valve if it has been dropped, damaged, or mishandled in any way. Should a bioprosthesis be damaged during insertion, do not attempt repair.

DO NOT HANDLE the leaflet tissue of the bioprosthesis with instruments or cause any damage to the valve tissue. Even the most minor tissue perforation may enlarge in time to produce significant impairment of valve function.

5. PRECAUTIONS
- The outside of the jar is not sterile and must not be placed in the sterile field.
- Adequate rinsing with physiological saline must be performed before implantation to reduce the glutaraldehyde concentration.
- Adequate removal of calcium deposits from the patient's annulus must be performed before implantation to avoid damage to the delicate prosthetic valve leaflet tissue as a result of contact with calcium deposits.
- Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure or breathing of the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with the eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, please refer to the Material Safety Data Sheet MSDI0424 available from Edwards Lifesciences.
- The Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 has a unique configuration designed to fit above the patient annulus rather than within the annulus. The surgeon should be familiar with the recommendations for proper sizing and placement in the Supraannular position. Refer to the **Device Implantation** section (11.3) for further details.

6. ADVERSE EVENTS

6.1. Observed Adverse Events

Two multi-center, non-randomized, prospective clinical studies were conducted. The first study was a long-term evaluation of 217 patients implanted with the Carpentier-Edwards S.A.V. Aortic Bioprosthesis Model 2650 and was conducted between 1991 and 1999. The second study was a short-term evaluation of 151 patients implanted with the Carpentier-Edwards S.A.V. Aortic Bioprosthesis Model 2650 between 1990 and 1994. There was an overlap of patients due to the enrollment period resulting in a pooled co-hort of 337 patients. In the long-term study, patients were evaluated preoperatively, intraoperatively/at discharge, and at periodic intervals thereafter. In the short-term study, patients were evaluated preoperatively, intraoperatively/at discharge, at 3 to 6 months, and at 1 year. Adverse events were captured throughout the postoperative period.

Table 1 presents the observed rates for early events (≤ 30 days for valve-related adverse events), the linearized rates for late events (>30 days postoperatively), and the cumulative freedom from adverse event rates at 1, 5, and 8 years postoperatively. The adverse event rates were based on 337 patients at 5 centers, with one center participating in both the long-term and short-term studies. The cumulative follow-up was 1392.9 patient-years with a mean follow-up of 4.1 years (SD=3.1 years, range=0 to 8.5 years).

Table 1: Observed Adverse Event Rates for AVR

All patients analyzed: N= 337 Cumulative follow-up: 1392.9 patient-years

Complication	Early Events		Late Events[1]		Freedom from Event (%) ± 95% CI[2]		
	n[3]	%	n	%/pt.-yr.	1 year (n = 269-281)	5 years (n = 137-153)	8 years (n = 24-31)
Mortality (all)	11	3.3	78	5.71	93.6 ± 2.8	74.1 ± 6.0	59.5 ± 13.3
Valve-related events							
Valve-related mortality	2	0.6	21	1.54	98.8 ± 1.3	92.1 ± 4.1	87.4 ± 10.9
Explant	0	0.0	5	0.37	99.4 ± 0.9	98.4 ± 2.0	97.2 ± 5.8
Reoperation[4]	0	0.0	0	0.00	100 ± 0.0	100 ± 0.0	100 ± 0.0
Bleeding	3	0.9	28	2.05	98.8 ± 1.3	91.5 ± 4.4	82.3 ± 12.6
Endocarditis	0	0.0	12	0.88	99.0 ± 1.1	97.0 ± 2.7	95.6 ± 7.1
Hemolysis	0	0.0	0	0.00	100 ± 0.0	100 ± 0.0	100 ± 0.0
Nonstructural dysfunction	0	0.0	2	0.15	99.7 ± 0.7	99.3 ± 1.4	99.3 ± 3.0
Perivalvular leak	0	0.0	3	0.22	99.7 ± 0.7	98.8 ± 1.8	98.8 ± 3.9
Structural valve deterioration	0	0.0	4	0.29	100 ± 0.0	99.5± 1.1	96.2 ± 6.6
Thromboembolism	6	1.8	36	2.64	96.5 ± 2.2	89.0 ± 5.0	83.3 ± 13.6
Valve thrombosis	0	0.0	0	0.00	100 ± 0.0	100 ± 0.0	100 ± 0.0

Notes:

1. Late event rates were calculated as linearized rates (%/pt-yr) based on 1366.2 late patient-years (>30 days postoperatively).
2. Freedom from event rates were calculated using the Kaplan-Meier method. Peto's formula was used for calculation of the 95% confidence intervals.
3. n = number of patients
4. Includes reoperation without valve explant.

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6.2. Potential Adverse Events

Adverse events potentially associated with the use of bioprosthetic heart valves include:

- Angina
- Cardiac arrhythmias
- Endocarditis
- Heart failure
- Hemolysis
- Hemolytic anemia
- Hemorrhage
- Myocardial infarction
- Prosthesis leaflet entrapment (Impingement)
- Prosthesis nonstructural dysfunction
- Prosthesis pannus
- Prosthesis perivalvular leak
- Prosthesis regurgitation
- Prosthesis structural deterioration
- Prosthesis thrombosis
- Stroke
- Thromboembolism

It is possible that these complications could lead to:

- Reoepration
- Explantation
- Permanent Disability
- Death

7. CLINICAL STUDIES

The safety endpoints captured in the prospective studies were adverse events. The safety results are provided above in Table 1. Effectiveness endpoints were New York Heart Association (NYHA) functional classification and echocardiographic assessments. Preoperative and operative patient demographics are presented below, followed by the effectiveness outcomes.

Table 2: Preoperative Patient Demographics

		Study Results (N = 1392.9 total pt-yrs)	
Variable	**Category**	**n**	**% (n/N)**
Age at Implant	Mean	337	70.2 ± 8.5
Gender	Female	138	41.0%
	Male	199	59.0%
NYHA Classification	I	3	0.9%
	II	92	27.3%
	III	197	58.5%
	IV	45	13.4%
Lesion	Stenosis	243	72.1%
	Insufficiency	35	10.4%
	Mixed	46	13.7%
	Malfunctioning prosthesis	13	3.7%

n = number of patients in each category; N = total number of study patients.

Table 3: Operative Patient Demographics

Variable	Category	Study Results (N=1392.9 total pt-yrs.)	
		n	% (n/N)[1]
Etiology[2]	Calcification/degeneration	253	75.1%
	Rheumatic heart disease	39	11.6%
	Congenital abnormalities	35	10.4%
	Other[3]	10	3.0%
Concomitant Procedures[2]	None	203	60.2%
	CABG[4]	115	34.1%
	AAA[5] repair/revision	10	3.0%
	Mitral valve repair	7	2.1%
	Other[6]	8	2.4%
Pre-existing Conditions[2]	Prior Myocardial Infarction	60	17.8%
	Chronic Lung Disease	126	37.4%
	Congestive Heart Failure	100	30.0%
	Arrhythmias	51	15.1%
	Systemic Hypertension	104	30.9%
Valve Size (mm)	19	14	4.2%
	21	76	22.6%
	23	115	34.1%
	25	89	26.4%
	27	37	11.0%
	29	4	1.2%
	31	2	0.6

Notes:
1. n = number of patients in each category; N = total number of study patients
2. May be more than one per patient
3. Includes previously failed prosthesis, remote endocarditis, and ischemic disease
4. CABG = Coronary Artery Bypass Graft
5. AAA=Ascending Aortic Aneurysm
6. Includes annulus enlargement, myectomy, pacemaker implant, IABP insertion, and aneurysm repair.

Table 4: Effectiveness Outcomes, Functional NYHA

NYHA Functional Class	Preoperative Assessment		Postoperative Assessments			
			1 Year[2]		4 to 5 Years[2]	
	N/N[1]	%	n/N	%	n/N	%
I	3/337	0.9%	157/309	50.8%	106/254	41.7%
II	92/337	27.3%	20/309	6.5%	18/254	7.1%
III	197/337	58.5%	2/309	0.6%	2/254	0.8%
IV	45/337	13.4%	0/309	0.0%	0/254	0.0%
Not Available	0	0.0%	130/309	42.1%	128/254	50.4%

Notes:
1. n = number of patients in each category; N = total number of study patients
2. Post-operative NYHA class percentages do not include explanted and deceased patients.

Table 5: Effectiveness Outcomes, Hemodynamic Results[1]

Hemodynamic Parameter	Results By Valve Size[1]						
	19mm[5]	21mm	23mm	25mm	27mm	29[5]mm	31[5]mm
Discharge (n = 122)							
Mean gradient[2]	N = 2	N = 29	N = 39	N = 32	N = 13	N = 2	N = 2
• mean ± sd	13.5 ± 12.0	12.6 ± 5.0	12.0 ± 5.5	10.4 ± 5.0	8.0 ± 5.2	5.1± 2.7	5.0 ± 2.5
• min, max	5, 22	4.9, 25	2.1, 35	3.1, 26	3, 23	3.2, 7.0	3.2, 6.7
EOA[3]	N = 2	N = 29	N = 38	N = 30	N = 11	N = 2	N = 2
• mean ± sd	0.56 ± .08	1.40 ± 0.47	1.58 ± .83	1.92 ± 0.65	2.01± 0.68	3.04 ± 1.20	2.20 ± 0.88
• min, max	0.51, 0.62	0.46, 2.89	0.80, 6.0	0.91, 3.80	1.00, 3.16	2.2, 3.89	1.56, 2.81
Regurgitation[4]	N = 3	N = 32	N = 40	N = 31	N = 13	N = 2	N = 2
0	3 (100.0%)	26 (81.3%)	35 (87.5%)	25 (80.6%)	13 (100.0%)	1 (50.0%)	1 (50.0%)
1+	0 (0.0%)	5 (15.6%)	4 (10.0%)	2 (6.5%)	0 (0.0%)	1 (50.0%)	0 (0.0%)
2+	0 (0.0%)	1 (3.1%)	1 (2.5%)	2 (6.5%)	0 (0.0%)	0 (0.0%)	1 (50.0%)
3+	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Not available	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1 Year (n = 115)							
Mean gradient[2]	N = 4	N = 27	N = 37	N = 29	N = 12	N = 2	N = 1
• mean ± sd	17.3 ± 2.6	12.7 ± 4.2	10.5± 4.3	11.3 ± 5.5	8.3 ± 3.3	4.2 ± 1.1	5.5 ± 0.0
• min, max	15, 21	4.6, 21.9	2.7, 24.5	3.7, 26.0	3.2, 15.2	3.4, 5.0	5.5, 5.5
EOA[3]	N = 4	N = 28	N = 35	N = 29	N = 12	N = 2	N = 1
• mean ± sd	0.75 ± 0.21	1.30 ±0.40	1.50 ± 0.40	1.70 ± 0.50	1.80± 0.60	2.30 ± 0.70	1.50 ± 0.00
• min, max	0.44, 0.92	0.80, 2.40	0.80, 2.58	0.8, 2.7	1.1, 3.2	1.8, 2.8	1.5, 1.5
Regurgitation[4]	N = 4	N = 30	N = 35	N = 28	N = 12	N = 2	N =1
0	4 (100.0%)	26 (86.7%)	30 (85.7%)	23 (82.1%)	10 (83.3%)	2 (100.0%)	1 (100.0%)
1+	0 (0.0%)	3 (10.0%)	2 (5.7%)	5 (17.9%)	2 (16.7%)	0 (0.0%)	0 (0.0%)
2+	0 (0.0%)	1 (3.3%)	2 (5.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
3+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Not available	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Notes:

1. Hemodynamic evaluations were performed using transthoracic echocardiography (TTE).
2. Mean gradient in mm Hg.
3. EOA: Effective Orifice Area, cm^2
4. Regurgitation: 0 = none; 1+ = trivial; 2+ = mild; 3+ = moderate; 4+ = severe
5. Sizes 19mm, 29mm and 31mm are not available in the United States because of insufficient data.

8. INDIVIDUALIZATION OF TREATMENT

Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial stages after implantation as determined by the physician on an individual basis. Long-term anticoagulant and/or antiplatelet therapy should be considered for patients with a dilated left atrium, a history of thrombotic events, an absence of sinus rhythm, calcification of the atrial wall, or with atrial fibrillation or flutter.

The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short-term and long-term risks and benefits to the patient and consideration of alternative methods of treatment.

8.1. Specific Patient Populations

The safety and effectiveness of the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 has not been established for the following specific populations because it has not been studied in these populations:

- patients who are pregnant;
- nursing mothers;
- patients with abnormal calcium metabolism (e.g., chronic renal failure, hyperparathyroidism);
- patients with aneurysmal aortic degenerative conditions (e.g., cystic medial necrosis, Marfan's syndrome);
- children, adolescents, or young adults.

9. PATIENT COUNSELING INFORMATION

Careful and continued medical follow up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed.

Patients with bioprostheses are at risk from bacteremia (e.g., undergoing dental procedures) and should be advised about prophylactic antibiotic therapy.

10. HOW SUPPLIED

10.1. Packaging

The Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 is chemically sterilized and supplied sterile and non-pyrogenic in a glutaraldehyde storage solution. Sterility is compromised if the package is opened, damaged, or the plastic seal applied to the jar is broken. The outside of the container is NOT sterile.

WARNING: Do not use if the valve container is leaking, damaged, or the glutaraldehyde solution does not completely cover the bioprosthesis.

10.2. Storage

Storage between 10°C and 25°C (50 and 77°F) is recommended. Do not freeze the bioprosthesis or expose to extreme heat. Each jar is shipped in a molded foam enclosure that contains a temperature indicator attached to the interior of the enclosure. If the temperature indicator has been activated, **do not use the bioprosthesis**. Immediately contact the local supplier or representative of Edwards Lifesciences to make arrangements for return and replacement. The molded foam and temperature indicator should be discarded after opening and inspecting, except in the case of an activated indicator.

The storage life of the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 is four (4) years from the date of sterilization. Appropriate inventory control should be maintained so that bioprostheses with earlier expiration dates are preferentially implanted and expiration is avoided.

11. DIRECTIONS FOR USE

11.1. Physician Training

No special training is required to implant the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650. The techniques for implanting this bioprosthesis are similar to those used for supraannular placement of any stented aortic bioprostheses.

11.2. Handling and Preparation Instructions

The bioprosthesis, integral holder, and the glutaraldehyde solution are sterile. The outside of the jar is not sterile and must not be placed in the sterile field. The contents of the jar should be handled in an aseptic manner to prevent contamination.

Examine the lid seal to verify that the bioprosthesis container has not been damaged or previously opened. Remove the seal and turn the lid counter-clockwise to open the container. The bioprosthesis, retainer, and holder within the container are sterile.

WARNING: Do not use the valve if it has been dropped, damaged, or mishandled in any way. Should a bioprosthesis be damaged during insertion, do not attempt repair.
WARNING: Do not handle the tissue portion of the bioprosthesis with instruments or cause any damage to the valve tissue. Even the most minor tissue perforation may enlarge in time to produce significant impairment of valve function.

Using the sterile gloved hand or protected forceps, grasp the projecting tab of the plastic retainer. The leaflet tissue should never be handled. Remove the plastic retainer, the integral holder, and the valve from the jar as an assembly.

A tag with a serial number is attached to each valve by a suture. This serial number should be checked against the number on the jar and implantation card; if any differences are noted, the valve should be returned unused. This tag should not be detached from the valve until just prior to implantation.

Two handles are available for attachment to the valve holder: the Model 1111 reusable handle, and the Model 1126 sterile, disposable handle. If using the Model 1111 handle, verify that it has been sterilized as per the instructions provided in the **Accessories Sterilization** section (11.5). If sterile, using handle Model 1111 or Model 1126, attach the handle to the valve by grasping the retainer at its outer edge as shown in Figure 2. **Do not grasp the valve.** Attach the handle by rotating the retainer or the handle. Tighten until positive contact is felt between the handle and holder.

An alternative method is to attach the handle to the valve holder while the valve is still in the container. To do this, simply insert the handle into the valve holder and turn it clockwise until it fits snugly. Be careful not to exert so much pressure while turning that the valve is pushed off the retainer ring and the tissue is damaged.

Once the handle has been attached, it should not be removed from the holder until after implantation has been completed and the handle/rotator assembly has been detached as a unit and removed from the operating field.

Remove the retainer by grasping the retainer edge and tab together and pulling towards you at an angle (**Figure 3**). Discard the retainer.

Rinse Procedure

Within the sterile operative field, prepare three rinse basins, each containing no less than 300 mL of sterile, physiological saline solution. Place the bioprosthesis in the saline solution and make sure that it completely covers the bioprosthesis and holder. With the valve and holder submerged, slowly agitate the basin (or use the attached handle to **gently** swirl the valve back and forth) for a minimum of 2 minutes in each of the three (3) previously prepared rinse basins. The bioprosthesis should remain in the third rinse basin until ready for implantation.

Caution: Avoid contact of the tissue or the rinse solution with towels, linens, or other sources of lint and particulate matter that may be transferred to the tissue.

Caution: Do not allow the tissue to contact the bottom or sides of the rinse basin.

Caution: Care must be taken to ensure that the serial number tag does not come in contact with the tissue during rinsing.

Inspection of the valve and removal of the serial number tag should be performed just prior to implantation. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal of the serial number tag.

11.3. Device Implantation

Sizing and Implantation Considerations

Proper bioprosthesis size selection is an important part of heart valve replacement. Care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the valve that may render it incompetent.

The size of the bioprosthesis is determined using the Carpentier-Edwards TRUE-SIZE sizers, Model 1166 aortic (**Figure 4**). The sizer is comprised of stainless steel and has two ends. One end is a cylindrical disc for sizing the patient annulus and is labeled 'Sizing'. The other end is a replica of the bioprosthesis for determining the desired Supraannular placement of the valve and is labeled 'Orientation'. Verify that the sizer has been sterilized as per the recommended instructions in the **Accessories Sterilization** section (11.5).

During implantation, the bioprosthesis should be periodically irrigated (every 1 to 2 minutes) with sterile physiologic saline on both sides of the valve to prevent drying of the tissue.

Implantation Procedure

Surgeons implanting the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 should be experienced in the implantation techniques required for supraannular implantation of prosthetic aortic valves. In general, the following steps should be used:

1. Surgically remove the diseased or damaged leaflets and all associated structures deemed necessary by the surgeon.

2. Surgically remove any calcium from the annulus to ensure proper suture placement and positioning of the valve.

3. Select the appropriate bioprosthesis size and orientation, using only Carpentier-Edwards TRUE-SIZE sizers, Model 1166 aortic:

    a. The actual size of the prosthesis to be implanted is determined by measuring the patient's aortic tissue annulus diameter using the disc-shaped end of the Model 1166 sizer (labeled 'Sizing'). This tissue annulus size is the same size as the tissue within the superstructure of the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 to be implanted. To size the annulus, simply insert the disc-shaped end of the Model 1166 sizer into the annulus. The sizer should fit comfortably.

    Caution: Do not use the replica-shaped end of the Model 1166 sizer to determine the **size** of the prosthetic valve to be implanted.

    b. The seating and orientation of the prosthesis to be implanted in the Supraannular space is determined using the replica-shaped end of the Model 1166 sizer (labeled 'Orientation'). This evaluation should follow, and not precede, sizing of the patient annulus. In all cases, the best orientation will leave the native coronary ostia unobstructed. To determine proper orientation, insert the replica-shaped end of the sizer into the patient annulus. Align the hash-marked cusp of the replica with the smallest intercommissural distance on the patient annulus. This same orientation will be used when implanting the bioprosthesis in step 5 below.

4. Rinse the bioprosthesis according to the instructions in the **Rinse Procedure** section (11.2) above.

5. Align the bioprosthesis on the annulus. The Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 features two suture marks on the area of the suture ring corresponding to the smallest cusp of the porcine valve. Align this suture-marked cusp of the bioprosthesis on the patient annulus in the same position identified by the replica-shaped end of the sizer in step 3b above.

6. Suture the bioprosthesis in place using an appropriate suturing technique.

Caution: Because the top of the suture ring is flush with the outflow of the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650, it is important to tie with pledgets the suture knots at the extreme outer periphery of the suture ring to avoid any contact between the suture tails with the leaflets during systole.

Caution: When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue.

Holder Removal
The integral holder and attached handle may be removed as a unit at the completion of the rinsing procedure as follows (**Figure 5**):

1. Using a scalpel or scissors cut each of the two exposed sutures that are on the surface of the holder. Avoid cutting or damaging the stent or leaflet tissue when cutting the sutures.

2. When all three attaching sutures have been properly cut, remove the handle/holder assembly, along with attaching sutures, from the valve as a unit.

3. Following surgery, remove the holder from the handle and discard the holder.

11.4. Accessories
All accessories are supplied non-sterile, except for the integral holder that is supplied sterile attached to the sterile bioprosthesis, and the Model 1126 single use handle that is supplied sterile for single use only.

Sizers
Use only the Carpentier-Edwards TRUE-SIZE aortic sizing obturator (Model 1166) to determine the appropriate Carpentier-Edwards S.A.V. Bioprosthesis Model 2650 size (**Figure 4**). Valve sizers are provided for each available bioprosthesis size.

Caution: Do not use other manufacturer's valve sizers or sizers for another Edwards Lifesciences prosthesis to size the Carpentier-Edwards S.A.V. Bioprosthesis Model 2650.

Valve Handle and Holder
The handle/holder assembly consists of two (2) components: the holder (an integral disposable part that is physically mounted to the valve by the manufacturer) and a handle (Model 1111 reusable handle or Model 1126) that is attached to the holder at the time of surgery.

11.5. Accessory Sterilization

The Model 1126 handle is supplied sterile and is for single use only. The Model 1111 handle and the Model 1166 sizers are supplied non-sterile and must be sterilized before using. The Model 1111 handle and the sizers must be disassembled, cleaned, and re-sterilized prior to each use. Sizers should be examined for signs of wear, cracking, etc.; and should be replaced if any deterioration is observed.

Caution: Do not sterilize the sizers or handles in their shipping containers.

The accessories can be sterilized using the following recommended autoclave sterilization methods:

I. Gravity Displacement
a) Wrapped:
Temperature: 270°-279°F (132°-137°C)
Exposure Time: 10-15 minutes
b) Unwrapped ("flash"):
Temperature: 270°F (132°C)
Exposure Time: 3 minutes

II. Prevacuum
a) Wrapped:
Temperature: 270°-279°F (132°-137°C)
Exposure Time: 3-4 minutes
b) Unwrapped ("flash"):
Temperature: 270°F (132°C)
Exposure Time: 3 minutes

Each institution should use procedures that include biological indicators to determine the effectiveness of the sterilization procedure.

11.6. Return of Explanted Bioprostheses

Edwards Lifesciences is interested in obtaining recovered Carpentier-Edwards S.A.V. Bioprosthesis Model 2650. Specific studies will be performed and a written report of our findings will be provided to the physician upon completion of our evaluation. Please contact your Edwards Lifesciences local valve specialist for information on the procedures to follow to return an explanted Carpentier-Edwards S.A.V. Bioprosthesis Model 2650. It is important that the explant be placed in a container of 10% formalin or 2% glutaraldehyde immediately after excision. Refrigeration is not necessary under these circumstances.

12. PATIENT INFORMATION

12.1. Registration Information

An *Implantation Data Card* is included in each device package for patient registration. After implantation, please complete all requested information. The valve serial number is listed on the valve packaging and on the identification tag attached to the bioprosthesis, and is pre-printed on the *Implantation Data Card.* Return the pre-addressed portion of the card to our Implant Patient Registry. The remaining portions of the card are provided for hospital and surgeon records. Upon receipt by our Implant Patient Registry, a wallet-sized identification card will be produced for the patient. This card allows patients to inform healthcare providers what type of implant they have when they seek care. When a valve is discarded or a previous Edwards Lifesciences device is replaced, report this information to our Implant Patient Registry.

12.2. Patient Manual

Patient information materials may be obtained from Edwards or an Edwards clinical sales specialist.

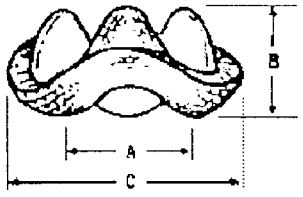
12.3. Magnetic Resonance Imaging (MRI) Compatibility

Testing of this device in a magnetic field of 1.5, 3.0 and 8.0 Tesla has shown that this device is safe and compatible during MRI (magnetic resonance imaging) procedures.

Figure 1

Specifications

Significant dimensions in millimeters (nominal values)



Model 2650 Aortic				
A. Mounting Diameter (Size) (Annulus)	21	23	25	27
B. Profile Height	15	16	17	17
C. External Diameter (Size)	28	30	32	34

Figure 2

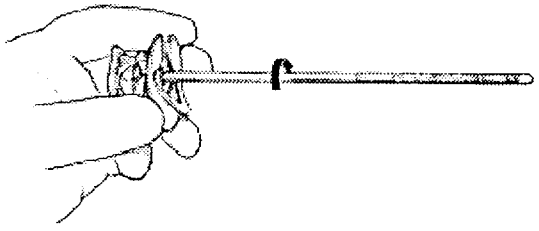


Figure 3

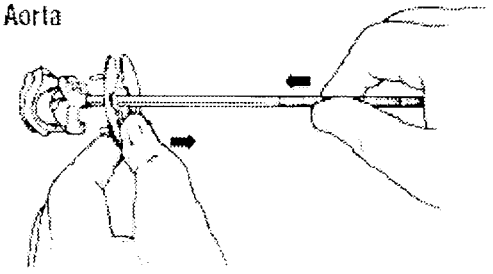
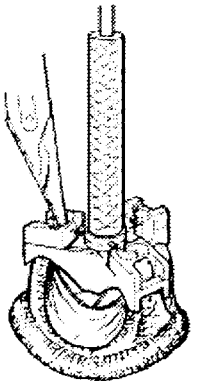


Figure 4

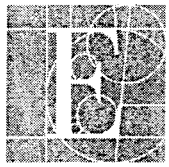
Figure 5



Prices subject to change without notice. This product is manufactured and sold under at least one or more of the following US patents: 4,451,936; 4,885,005, and corresponding foreign patents. Additional patents are pending.

HEART VALVE SURGERY

Information Every Patient Should Know



Edwards

Patients and Families

Introduction

The following information is intended for patients who may be facing heart valve surgery. Family members or friends of patients may also find this information useful. The information has been provided to help you understand the anatomy of the heart, how the heart and its valves function, how heart valve disease is diagnosed and potential treatment options.

Please remember, this information is not intended to tell you everything you need to know about artificial heart valves or heart valve repair products, or about related medical care. Regular check-ups by a heart specialist are essential and you are encouraged to call or see your doctor whenever you have questions or concerns about your health, especially if you experience any unusual symptoms or changes in your overall health. This information is not intended as a substitute for personal medical care and advice. Only your doctor can diagnose and recommend treatment for heart disease.

Prepared in consultation with Steven Bolling, M.D., University of Michigan Hospitals, Department of Thoracic Surgery, Ann Arbor, Michigan, USA

Glossary

myocardium - the fibrous muscle of the heart
oxygenated - combined with oxygen

orifice-annulus ratio – ratio of the valve opening area to the valve annulus diameter

pericardial valve - tissue valve made from bovine (cow) pericardial tissue

porcine valve - tissue valve made from pig's aortic heart valve

prosthetic – replacement device for part of the body

prothrombin time test – lab test to measure blot clotting time

pulmonary valve - the valve between the right ventricle and pulmonary artery

regurgitation - backward flow

semilunar valves - the aortic and pulmonary valves named for their three cusps shaped like half moons
sinus rhythm - when the heart contracts in a normal, coordinated manner

sinus rhythm – when the heart contracts in a normal, coordinated manner at a normal rate

stenosis - a narrowing of a valve opening

superior and inferior venae cavae - the two largest veins returning deoxygenated blood to the right side of the heart

systole - period of contraction in the cardiac cycle when the heart squeezes or pumps

tilting disc valve - mechanical valve with a single circular disc held in place within a housing but allowed to tilt open and closed at an angle, and also to rotate within that housing

tissue valve – replacement valve composed of biological tissue

tricuspid valve - the valve that separates the right atrium from the right ventricle

valves – structures in the body that regulate flow

veins - blood vessels which return blood to the heart

ventricles - the large lower pumping chambers of the heart

The Heart

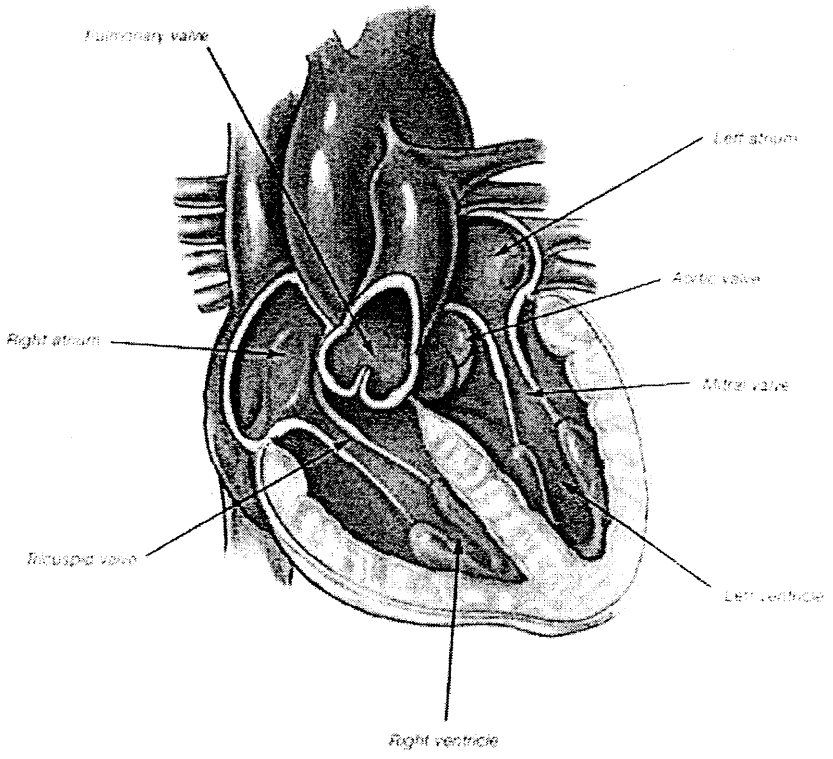


Figure 1-1: Chambers and Valves of the Heart

The Heart

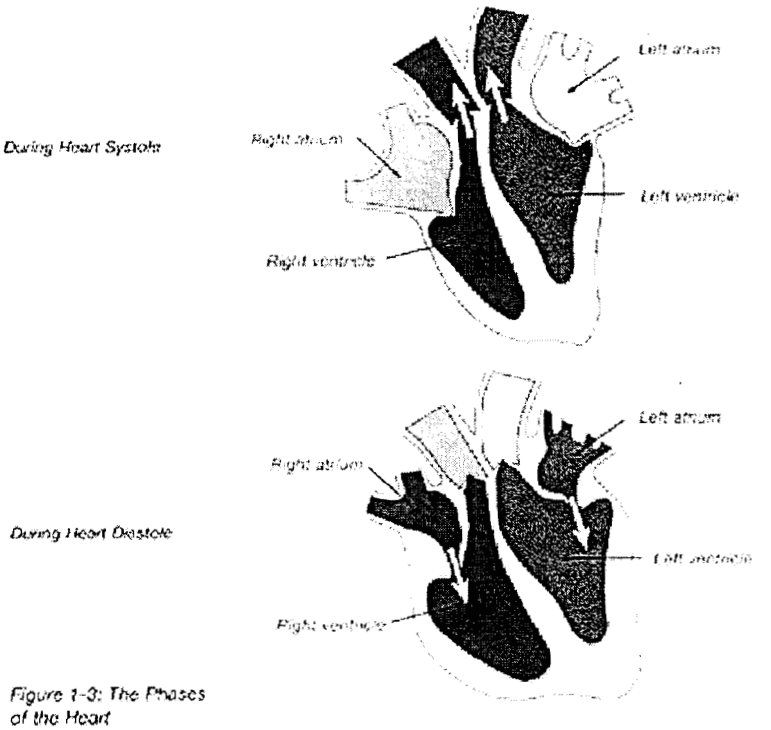


Figure 1-3: The Phases of the Heart

The Heart Muscle and Cardiac Cycle

The fibrous muscle of the heart (the myocardium) is important because it produces the forces needed to push blood from the ventricles. When the ventricles contract, they force blood out through valves and into the aorta or pulmonary artery. This phase of the heart cycle is referred to as systole. When the ventricles relax, blood flows into them from the atria. This phase is called diastole. See Figure 1-3.

The Heart

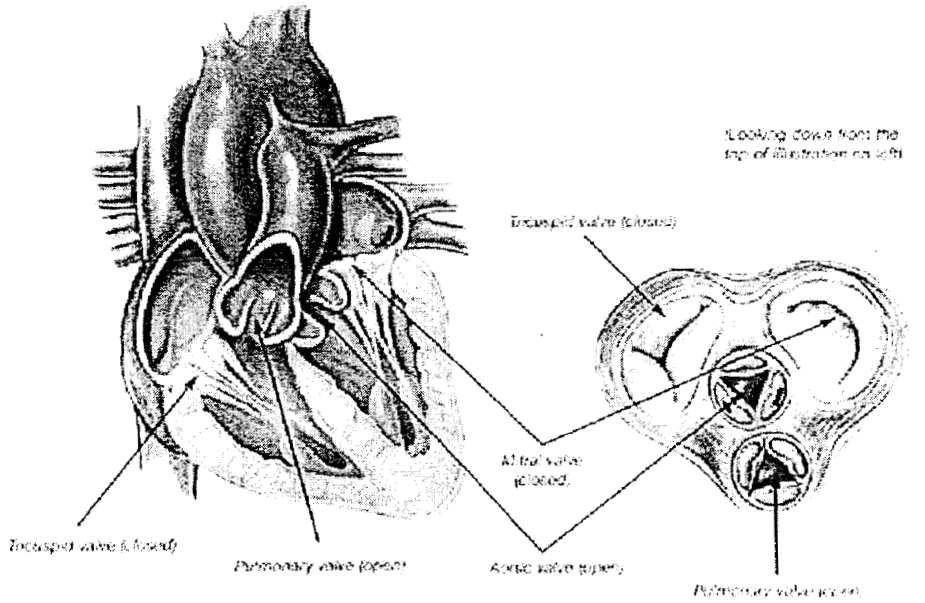


Figure 1-4: View of the Heart Valves

the right ventricle and pulmonary artery. The mitral and tricuspid valves are substantially larger than the aortic and pulmonary valves. Figure 1-4 shows the shape and location of the four heart valves

The characteristic heart sounds ("lubb, dubb") are caused by the closing of the heart valves, the first by closure of the mitral and tricuspid valves and the second by the closure of the aortic and pulmonary valves.

Valve Defects and Diagnosis

There are two common conditions that can occur when a natural heart valve becomes defective. They are:

- stenosis (valve narrowing)
- regurgitation (leaky valve)

This can occur in just one valve, or in more than one valve.

See Figure 2-1.

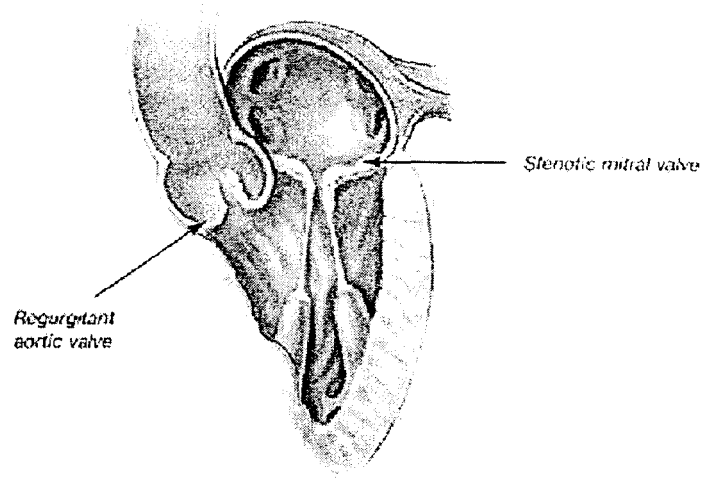


Figure 2-1: A leaky (regurgitant) aortic valve allows blood to flow back from the aorta to the left ventricle when the ventricle relaxes. A narrowed (stenotic) mitral valve restricts blood flow from the left atrium to the left ventricle.

Valve Defects and Diagnosis

time this increasing pressure gradually stretches the muscles of the chamber wall which respond by becoming thicker. The result is an enlarged heart. This condition should not be confused with the larger, stronger heart of, for example, an athlete. Rather, an enlarged heart simply means one with a stretched chamber and increased muscle mass. The possible complication with an enlarged heart is an increased likelihood of blood clots forming. The incidence of this complication increases because the blood that is backed up in the enlarged chamber is more stagnant. The more blood pools in one spot, the greater possibility for it to form a clot. This complication arises more frequently when the heart is not in sinus rhythm. (Recall that sinus rhythm refers to normal, coordinated contraction of heart muscles.)

Regurgitation (Insufficiency/Incompetence)

Regurgitation is the inability of a valve to close completely, which results in significant backward flow of blood through the valve. The major causes of regurgitation are rheumatic fever, bacterial endocarditis, coronary artery disease, and venereal disease.

There are three mechanisms by which infections can cause regurgitation. First, infections can cause lesions (scars or rough spots) on the flaps. This scar tissue can build up to the point where the cusps are so rigid (and stenotic) that they cannot close properly. This results in backflow through the valve. Thus, it is possible for a valve to be regurgitant in addition to being stenotic.

Second, infections may cause tissue to break down, tear, or form holes in the valves or around the perimeter of the valve (perivalvular leaks).

Third, blockage of a coronary artery due to coronary artery disease can cause papillary muscle dysfunction (inadequate or impaired function) due to a disruption in the supply of nutrients and oxygen to the muscle tissue. Papillary muscles are structures that contract to make the mitral and tricuspid valves open.

Infection and myocardial infarction can also cause other problems with the supporting valve structures that cause problems with valve closure. As in stenosis, regurgitation can progress through stages of severity over time, resulting in worsening of the condition and onset of the symptoms.

Generally, even though the initial damage to a valve may happen early in life, the early effects are mild and the defect progresses slowly. Although some regurgitation occurs with all valves, when the regurgitation rate attains a significant level, clinical problems may become noticeable and symptoms are felt by the patient.

Valve Defects and Diagnosis

Echocardiography

Echocardiography is a special application of ultrasound. Ultrasound waves that are sent into the body detect the echoes bouncing back from the heart's structures. A computer translates the sound waves into an image. Another type of echo is transesophageal echo in which a tube with an ultrasound probe is inserted down the throat near the heart.

Catheterization

Cardiac catheterization (angiography) helps to determine the function of the coronary arteries and the heart valves. Cardiac catheterization is the process by which a tube is inserted into the blood vessels and/or heart. The tube injects a contrast medium (dye) that is then visualized with X-rays. Coronary angiography is particularly useful for analyzing the coronary vessels of the heart.

Valve Treatment

Valve Replacement

When your heart valve is severely diseased, your doctor may choose to replace it. If so, the first step is to remove the diseased valve (excise the valve) and then implant a prosthetic heart valve in its place. Prosthetic valves used to replace the diseased natural valves come in different sizes to fit your anatomy and are made of a variety of materials.

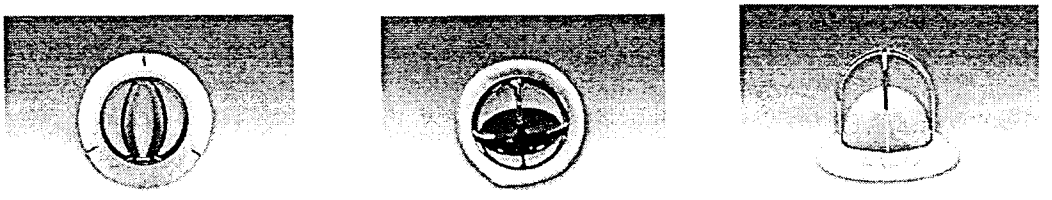
There are two broad categories of heart valves that are classified according to the type of material:

- bioprosthetic or tissue valves made primarily from animal tissue [i.e., a pig's aortic valve, a cow's pericardium (sac surrounding its heart) or human valves from cadavers]
- mechanical valves constructed from synthetic material

Valve Treatment

Mechanical Valves

There are three basic types of mechanical valves. A bileaflet valve has two semicircular discs (referred to as leaflets) that are mounted on hinges within a housing and open and close simultaneously. A tilting disc valve has a housing with a single circular disc that tilts open and closed. The disc is typically supported by "struts." The ball and cage design has a spherical ball that moves within a cage.



tilting disc *bileaflet valve valve* *ball and cage valve*

Figure 3-3: Mechanical Valves

Care After Surgery

The normal recovery period from heart surgery occurs during the first four to six weeks after the surgery. Typically during this time patients begin to restore muscle tone and return to normal levels of activity. The following information may be helpful for patients who have had their natural heart valves replaced or repaired with an artificial heart valve or annuloplasty device. This information has been provided to help you understand the heart surgery, the prosthesis, and life with the new heart valve prosthesis or about related medical care. Regular check-ups by a heart specialist are essential and you are encouraged to call or see your doctor whenever you have questions or concerns about your health, especially if you experience any unusual symptoms or changes in your overall health.

Diet and Exercise

Two important parts of recovery and continuing health are a good diet and a regular exercise program. If your doctor has recommended a special diet, it is important that it be followed; however, if a special diet has not been recommended, the information listed below can provide guidance to balanced eating which may speed healing and lessen fatigue. In addition, the practice of weight control is important in reducing the work of the heart even after recovery.

Balanced eating is necessary because no one food provides all the nutrients needed by the body; therefore, each day a variety of fruits, vegetables, whole grains, breads, meats and dairy products should be eaten.

Foods that are high in saturated fats, sugar, salt, and sodium should be limited. In general, a low fat, low cholesterol, high fiber diet is best. Use of supplemental calcium should not be taken without approval from your doctor. To improve overall cardiovascular fitness, it is recommended that you combine a balanced diet with your doctor's recommendations about exercise and weight control. Following a regular exercise program is an important part of maintaining a healthy lifestyle. Under your doctor's guidance, you should gradually build up your exercise and activity level. Before you begin a new sports activity, check with your doctor.

Anticoagulants

It is important to carefully follow your doctor's directions for taking medications, especially if an anticoagulant drug has been prescribed. This type of drug decreases the blood's natural ability to clot or coagulate and is sometimes called a blood thinner. Those who take anticoagulant drugs need a prothrombin time test (commonly called a pro-time test) every two to four weeks. A pro-time test measures the level of certain clotting factors that indicate the blood's ability to clot. This test result helps the doctor determine the amount of anticoagulant needed. The pro-time test should be done at the same lab every time because results may vary from one lab to another. It may take a while to establish the right dosage for each person, but consistency and working with your doctor are important. Home testing may be available, so check with your physician about this option.

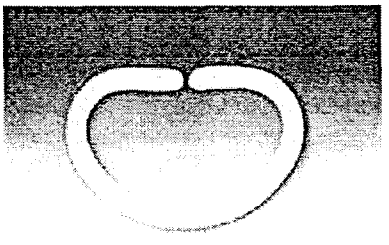
Edwards Annuloplasty Products

Carpentier-Edwards Classic Annuloplasty Rings

The Carpentier-Edwards Classic Annuloplasty Ring was first introduced in 1968. The first implants were at the Hospital Broussais in Paris by Prof. Alain Carpentier. The ring was manufactured and distributed by the French company, Rhone-Poulenc. In 1980, Edwards Laboratories (now Edwards Lifesciences) took over manufacturing and distribution rights of the annuloplasty ring. Originally made from stainless steel, the core of the ring was changed to titanium in 1983. The reason for the change was the increased strength of the titanium metal over stainless steel and complexity of forming the stainless steel rings. The name "Classic" was introduced in 1995 to reinforce its history as the ring of choice for thousands of surgeons since 1968.

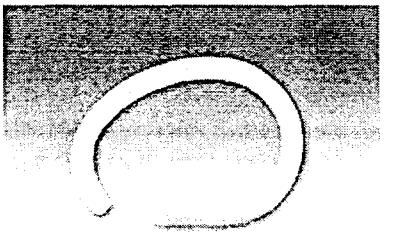
Description

The Carpentier-Edwards Classic Annuloplasty Ring is available in two designs: a kidney shaped mitral ring (Models 4400/4425) and an oval tricuspid ring (Models 4500/4525).



Carpentier-Edwards Classic Annuloplasty Ring
Mitral Models 4400/4425

The oval tricuspid ring (Models 4500/4525) conforms to the configuration of the normal tricuspid opening. The ring is open at the lower left section so that sutures do not need to be placed in this area to avoid causing cardiac rhythm disturbances. The Carpentier-Edwards Classic Annuloplasty Rings are constructed of titanium alloy covered by a layer of silicone rubber. The ring is then covered with a polyester knit fabric.



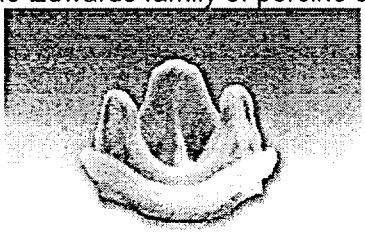
Carpentier-Edwards Classic Annuloplasty Ring
Tricuspid Models 4500/4525

Edwards Stented Porcine Valve Products

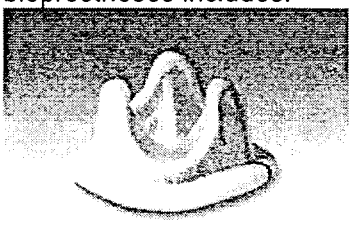
Introduction

Between 1968 and 1973, the Carpentier-Edwards bioprosthetic porcine valve was introduced. In 1970, a clinical evaluation of Carpentier-Edwards valves was conducted. The first Carpentier-Edwards bioprosthesis incorporating a special preservation method was implanted by Prof. Alain Carpentier in 1975. This valve was released for general use one year later. In 1982, the Carpentier-Edwards S.A.V. (supra-annular valve) Bioprosthesis was introduced outside the USA.

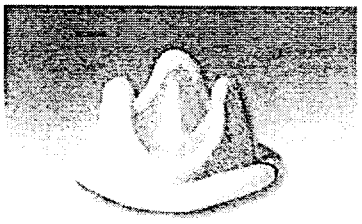
The Edwards family of porcine stented bioprostheses includes:



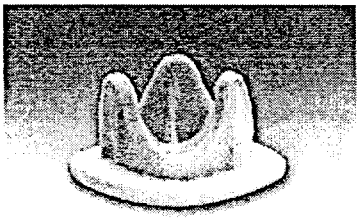
Carpentier-Edwards Bioprosthesis Aortic Model 2625



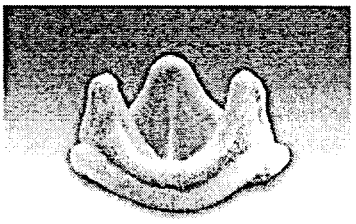
Carpentier-Edwards Bioprosthesis Mitral Model 6625



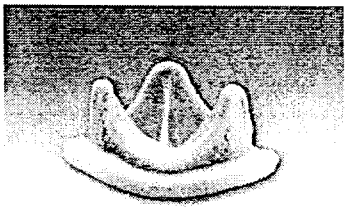
Carpentier-Edwards Duraflex Low Pressure Bioprosthesis Mitral Model 6625-LP
(Available in the USA only)



Carpentier-Edwards Duraflex Low Pressure Bioprosthesis Mitral Model 6625-ESR-LP
(Available in the USA only)



Carpentier-Edwards S.A.V. Bioprosthesis Aortic Model 2650



Carpentier-Edwards S.A.V. Bioprosthesis Mitral Model 6650
(Available outside the USA only)

Carpentier-Edwards Bioprostheses are comprised of pig aortic valves that have been "fixed" in a preservation liquid and then mounted on flexible frames. The frame is designed to be flexible at the opening as well as where the leaflets come together. The frame is covered with a porous, knitted polytetrafluoroethlyene (PTFE) cloth. A sewing ring made of molded silicone rubber covered by polytetrafluoroethylene cloth enables the surgeon to sew the valve into the patient.

Edwards Pericardial Valve Products

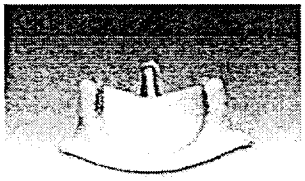
Introduction

In 1979, Professor Carpentier and Edwards Lifesciences began the development of a pericardial valve in an attempt to improve upon the earlier pericardial valve designs. The aortic Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis was introduced internationally in 1980, and in the United States in October of 1991. The pericardial valve is a biomechanically engineered valve that can be described as a mechanical valve with a biologic component. In this way, it differs from a porcine (pig) stented valve that incorporates a natural pig's valve.

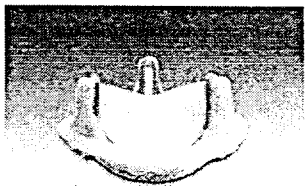
There are several aortic models available. The U.S. models are the Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis (Model 2700) and the Carpentier-Edwards PERIMOUNT RSR (reduced sewing ring) Pericardial Bioprosthesis (Model 2800). The international model is the Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis (Model 2900).

In addition, there are two mitral models of the PERIMOUNT valve. The Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis (Model 6900) and the Carpentier-Edwards PERIMOUNT Plus Pericardial Bioprosthesis (Model 6900P).

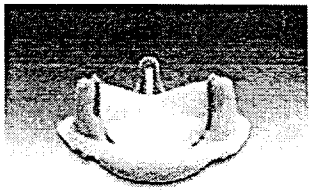
The Carpentier-Edwards PERIMOUNT Bioprostheses are constructed from three pieces of bovine (cow) pericardial tissue. Tissue is cut out from a carefully selected region of cow tissue surrounding the heart. The tissue is mounted on a lightweight frame that is covered with a porous, knitted polytetrafluoroethylene (PTFE) cloth. A sewing ring made of molded silicone rubber covered by polytetrafluoroethylene cloth enables the surgeon to sew the valve into the patient.



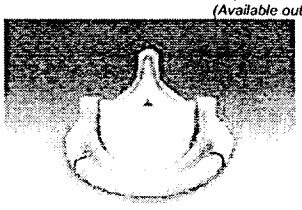
Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis Aortic Model 2700 (Available in the USA only)



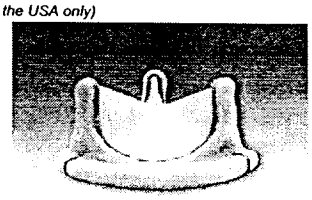
Carpentier-Edwards PERIMOUNT RSR Pericardial Bioprosthesis Aortic Model 2800 (Available in the USA only)



Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis Aortic Model 2900 (Available outside the USA only)

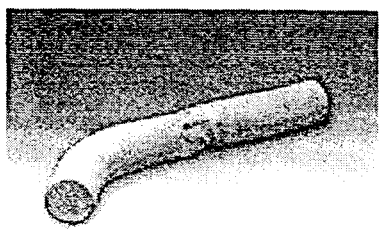


Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis Mitral Model 6900



Carpentier-Edwards PERIMOUNT Plus Pericardial Bioprosthesis Mitral Model 6900P

Edwards Valved Conduit



Carpentier-Edwards
Bioprosthetic Valved Conduit Model 4300

The Carpentier-Edwards Bioprosthetic Valved Conduit (Model 4300) is made from a porcine (pig) aortic valve that has been preserved and mounted on a flexible frame. The flexible frame is composed of a corrosion resistant cobalt chromium metal alloy, silicone rubber, and is covered with polytetrafluoroethylene (PTFE) cloth. The valve is then mounted in a polyester tube. This device can be used to create an extra-cardiac pathway for blood flow in the pulmonic position. This conduit was introduced in the 1970's.

Frequently Asked Questions

How long does an artificial heart valve last?

Longevity of an artificial tissue valve depends on many patient variables and medical conditions. This makes it impossible to predict how long a valve or repair device will last in any one patient. However, symptoms indicating that a tissue valve may need replacement typically occur over time and allow the doctor to schedule elective surgery, if the need arises.

It is recommended that patients have regular checkups with their doctors to monitor the performance of their heart valve prosthesis. Your doctor is familiar with your medical history, your current condition, and the medication you are taking. Therefore, he or she is in the best position to answer specific questions about your valve.

Can an artificial heart valve be fixed if it wears out?

Reoperation to repair replacement valves (or annuloplasty devices) is quite variable and depends on the reason for the repair. If a valve is calcified, it probably would be replaced with a new valve. Your surgeon would be in the best position to answer specific questions about your valve.

Bovine or Porcine Tissue?

Artificial tissue heart valves are typically made from either bovine pericardium or porcine tissue. Bovine refers to cow or cattle, whose pericardial tissue is used to make the valve. Pericardium is a thick fibrous membrane that surrounds the heart. Porcine refers to pig, whose aortic heart valve tissue is used to make the valve.

The Edwards porcine valve has been marketed since 1975. The Edwards bovine aortic valve was first used in clinical trials in humans in 1981 and was approved for sale in the USA in 1991. Your surgeon is in the best position to discuss treatment options with you.

How do I take care of my valve?

- Be sure your doctors and dentist know that you have had heart valve surgery.
- Ask your dentist and doctor about taking antibiotics before dental or surgical procedures to help prevent valve infection.
- Avoid excessive amounts of calcium if you have a tissue valve.
- Follow your doctor's instructions.

Notes