

# 1994 ANNUAL MEETING PROGRAM



## THE AMERICAN ASSOCIATION FOR THORACIC SURGERY 1993-1994

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## POSTGRADUATE COURSE

<p><b>AATS Postgraduate Course Congenital Heart Disease</b></p> <p><b>Sunday, April 24, 1994 8:00 a.m. - 4:00 p.m.</b></p> <p><b>New York Hilton Hotel New York, New York</b></p>	<p><b>Objectives</b></p> <p>The 1994 Postgraduate Course on Congenital Heart Disease will address the following three topics: Surgical Techniques, Postoperative Care - Issues for the 1990s and Pediatric Lung Transplantation. This course will provide attendees with the opportunity to interact with recognized experts involved in the research and development of new techniques and procedures in congenital heart disease. The format of the course will include video presentations and lectures on current issues within each of the three topic areas, with ample time provided during each session for discussion of specific questions from the audience.</p> <p><b>Registration</b></p> <p>Enrollment in this course will be by pre-registration until March 25, 1994. After March 25, 1994, participants may register on site at the Hilton Hotel in New York. The registration fee is \$50.00 and includes the PG course, coffee break, and lunch. Special convention rates have been obtained at the Hilton and Towers Hotel in New York, New York.</p> <p><b>Accreditation</b></p> <p>The American Association for Thoracic Surgery is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. The American Association for Thoracic Surgery designates this continuing medical education activity for 6 credit hours in Category I of the Physicians Recognition Award of the American Medical Association.</p>
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## **SUNDAY, APRIL 24, 1994**

Program - Trianon Ballroom

7:00 a.m. REGISTRATION/CONTINENTAL BREAKFAST

### **SESSION I SURGICAL TECHNIQUE - VIDEO PRESENTATIONS**

7:50 a.m. INTRODUCTORY REMARKS

*Edward L. Bove, M.D., Chairman*

*Robert M. Sade, M.D., Co-Chairman*

8:00 a.m. THE ARTERIAL SWITCH PROCEDURE

*Constantine Mavroudis, M.D., Chicago, Illinois*

8:20 a.m. TRANSATRIAL REPAIR OF TETRALOGY OF FALLOT

*Albert D. Pacifico, M.D., Birmingham, Alabama*

8:40 a.m. THE NORWOOD PROCEDURE

*Edward L. Bove, M.D., Ann Arbor, Michigan*

9:00 a.m. THE HEMIFONTAN PROCEDURE

*Robert M. Sade, M.D., Charleston, South Carolina*

9:20 a.m. THE FONTAN PROCEDURE

*Hillel Laks, M.D., Los Angeles, California*

9:40 a.m. DISCUSSION

10:15 a.m. REFRESHMENT BREAK

### **SESSION II POSTOPERATIVE CARE - ISSUES FOR THE 1990s**

10:45 a.m. NITRIC OXIDE FOR PULMONARY HYPERTENSION

*David I. Wessel, M.D. Boston, Massachusetts*

11:00 am. MANAGEMENT OF THE POSTOPERATIVE NORWOOD PATIENT

*Thomas J. Kulik, M.D. Ann Arbor, Michigan*

11:15 a.m. ECMO/LEFT VENTRICULAR ASSIST

*Pedro J. del Nido, M.D., Pittsburgh, Pennsylvania*

11:30 a.m. ULTRAFILTRATION AND FLUID MANAGEMENT FOLLOWING  
CARDIOPULMONARY BYPASS

*Martin J. Elliot, M.D., F.R.C.S., London, England*

11:45a.m. DISCUSSION

12:15 p.m. LUNCHEON

### **SESSION III PEDIATRIC LUNG TRANSPLANTATION**

2:00 p.m. DIAGNOSIS AND MANAGEMENT OF REJECTION AND INFECTION

*Thomas L. Spray, M.D., St. Louis, Missouri*

2:15 p.m. PULMONARY HYPERTENSION - WHICH TRANSPLANT?

*John Armitage, M.D., Pittsburgh, Pennsylvania*

2:30 p.m. COMBINED HEART AND LUNG TRANSPLANTATION

*Bruce A. Reitz, M.D., Stanford, California*

2:45 p.m. SINGLE LUNG TRANSPLANTATION IN CHILDREN

*Vaughn A. Starnes, M.D., Los Angeles, California*

3:00 p.m. LUNG TRANSPLANTATION FOR CYSTIC FIBROSIS

*Thomas M. Egan, M.D., Chapel Hill, North Carolina*

3:15 p.m. DISCUSSION

4:00 p.m. MEETING ADJOURNS



## DEVELOPING THE ACADEMIC SURGEON SYMPOSIUM

<p><b><i>AATS/STS</i></b> <b>2nd</b> <b>International</b> <b>Symposium</b> <b>on</b> <b>Thoracoscopy</b> <b>and Video</b> <b>Assisted</b> <b>Thoracic</b> <b>Surgery:</b> <b>Technology</b> <b>on Trial</b></p> <p><i>Sunday, April 24, 1994</i> <b>8:00 a.m. -4:30 p.m.</b></p> <p><b>New York Hilton Hotel</b> <b>New York, New York</b></p>	<p><b>Objectives</b> Discuss in a debate format the changes in general thoracic surgery from the introduction of video assisted thoracic surgery. Lively discussion will help formulate the appropriate role for the this technology in our specialty.</p> <p><b>Registration</b> Enrollment in this Symposium will be by pre-registration until March 25, 1994. After March 25, 1994, participants may register on site at the Hilton Hotel in New York. The registration fee is \$100.00 and includes the Symposium, coffee breaks, and lunch. Special convention rates have been obtained at the Hilton and Towers Hotel in New York, New York.</p> <p><b>Accreditation</b> The American Association for Thoracic Surgery is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. The American Association for Thoracic Surgery designates this continuing medical education activity for 7 credit hours in Category I of the Physicians Recognition Award of the American Medical Association.</p>
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## SUNDAY, APRIL 24, 1994

### PROGRAM - WEST BALLROOM

7:00 a.m. REGISTRATION/CONTINENTAL BREAKFAST

8:15 a.m. INTRODUCTION

The Assessment of New Technology in Thoracic Surgery

*Martin F. McKneally, M.D.*

#### SESSION I

***Panelists: Martin F. McKneally, M.D., Geoffrey Graeber, M.D., Paolo Macchiarini, M.D.***

8:30 a.m. VIDEO ASSISTED THORACIC SURGERY EVALUATION OF THE INDETERMINATE PULMONARY NODULE INSTEAD OF NEEDLE ASPIRATION BIOPSY

*PRO: Michael Mack. M. D. CON: Willard Fry. M.D*

9:00 a.m. LOBECTOMY SHOULD BE PERFORMED BY VIDEO ASSISTED THORACIC SURGERY

*PRO: Giancarlo Roviario, M.D. CON: Peter C. Pairolero. M.D*

9:30 a.m. VIDEO ASSISTED THORACIC SURGERY MANAGEMENT OF LUNG CANCER

*PRO: Ralph J. Lewis, M. D. CON: L Penfield Faber. M. D.*

10:00 a.m. COFFEE BREAK

#### SESSION II

***Panelists: Stephen Hazelrigg, M.D., Thomas W. Shields, M.D., Richard G. Fosburg, M.D.***

10:30 a.m. VIDEO ASSISTED THORACIC SURGERY EVALUATION OF MEDIASTINAL LYMPHADENOPATHY

*PRO: Larry R. Kaiser. M.D. CON: Robert J. Ginsberg, M.D*

11:00 a.m. VIDEO ASSISTED THORACIC SURGERY MANAGEMENT OF PULMONARY METASTASES

*PRO: Rodney Landreneau. M.D. CON: Valerie W. Rusch*

11:30 p.m. LUNCHEON AND DISCUSSION

What have we learned so far about video assisted thoracic surgery?

*Joel D. Cooper, M.D. and David S. Mulder, M.D.*

#### SESSION III

***Panelists: Jean Deslauriers, M.D., Joel D. Cooper, M.D., Mark K. Ferguson, M.D.***

1:00 p.m. VIDEO ASSISTED THORACIC SURGERY MANAGEMENT OF BULLOUS EMPHYSEMA

*PRO: Akin Wakabayashi, M.D. CON: Tom Kirby, M.D*

1:30 p.m. VIDEO ASSISTED MYOTOMY AND FUNDOPLICATION

*PRO: Tom R DeMeexler, M.D. (myotomy) CON: Mark R. Orringer, M.D.*

*PRO: Robert Keenan, M.D (Fundoplication) (Myotomy and Fundoplication)*

2:10 p.m. VIDEO ASSISTED THORACIC SURGERY THYMECTOMY FOR MYASTHENIS GRAVIS

*PRO: David Sugar/taker. M.D. CON: G. Alec Patterson. M.D.*

2:40 p.m. COFFEE BREAK

#### **SESSION IV**

*Panelists: Thomas Daniel, M.D., Joseph LoCicero, M.D., Ralph J. Lewis, M.D.*

3:10 P.M. COMPLICATIONS SPECIFIC TO VIDEO ASSISTED THORACIC SURGERY

*Joseph I. Miller. M.D.*

3:30 p.m. VIDEO ASSISTED THORACIC SURGERY PERICARDIECTOMY

*PRO: Stephen Hazelrigg, M.D. CON: Keith Naunheim M.D.*

4:00 p.m. IT IS APPROPRIATE FOR PULMONOLOGISTS TO PERFORM THORACOSCOPY FOR PLEURAL DISEASE

*PRO: William Martin, M.D. CON: Martin F. McKneally, M.D.*

4:30 p.m. CLOSING REMARKS

*Michael Mack. M.D.*

**American Association for  
Thoracic Surgery  
74th ANNUAL MEETING  
New York Hilton Hotel, New York, NY  
APRIL 24-27, 1994**

**MONDAY MORNING, April 25, 1994**

**8:30 a.m. BUSINESS SESSION (Limited to Members)**

**8:45 a.m. SCIENTIFIC SESSION - Grand Ballroom**

**Moderators: Aldo R. Castaneda, M.D.  
James L. Cox, M.D.**

**1. POSTINTUBATION TRACHEAL STENOSIS: LATE RESULTS OF SURGICAL TREATMENT**

Hermes C. Grille, M.D., Dean M. Donahue, M.D.\*, Douglas J. Mathisen, M.D.,

Cameron D. Wright, M.D.\* and John C. Wain, M.D.\*

*Boston, Massachusetts*

493 patients underwent 505 tracheal resections and reconstructions for postintubation stenosis from 1965 to 1992. 52 had had prior attempts at surgical resection, 52 others had undergone various forms of tracheal or laryngeal repair, and 40 laser treatment. There were 248 cuff lesions, 174 stomal lesions, 36 at both levels, and 35 of indeterminate origin. 60 with major laryngeal injuries required complete resection of anterior cricoid cartilage and anastomosis of trachea to thyroid cartilage, and 111 had partial anterior cricoid resection. Cervical approach was used in 343, cervicomedial in 144, and transthoracic in 6. Length of resection was 1.0 cm - 7.5 cm. 44 had laryngeal release to reduce anastomotic tension.

449 patients (91%) showed good (86%) or satisfactory (5%) results. 12 of 17 who failed underwent repeat reconstruction. 12 required postoperative tracheostomy or T-tube for extensive or multilevel disease. 15 died (3%). The most common complication, suture line granulations (9.5%), has almost vanished with use of absorbable sutures. Wound infection occurred in 15 (3%), and glottic dysfunction in 11 (2.2%). 3 had postoperative innominate artery hemorrhage. Resection and reconstruction offers optimal treatment for postintubation tracheal stenosis.

\*By invitation

## **2. EFFECTS OF HYPOTHERMIC CIRCULATORY ARREST ON NEUROLOGIC AND DEVELOPMENTAL OUTCOME AT AGE ONE YEAR**

Richard A. Jonas, M.D., Gil Wernovsky, M.D.\*, David C. Bellinger, Ph.D.\*, Leonard A. Rappaport, M.D.\*, Karl C. Kuban, M.D.\*, Patrick Barnes, M.D.\*, Roy Strand, M.D.\*, David Wypij, Ph.D.\* and Jane W. Newburger, M.D.\*

*Boston, Massachusetts*

We compared neurologic and developmental status at age 1 yr in patients with D-TGA who had been enrolled before their arterial switch operation in a prospective, randomized trial comparing deep hypothermia with predominantly circulatory arrest (CA) vs. predominantly low-flow cardiopulmonary bypass (LF). Neurologic exam, developmental testing, and magnetic resonance (MR) interpretations were performed by blinded investigators. One-year assessments were available in 155 patients (91% of those enrolled).

Abnormalities on neurologic examination tended to be more common among infants randomized to the CA strategy ( $p=.057$ ). Similarly, neurologic abnormalities were significantly associated with longer duration of CA ( $p = .018$ ). Specific abnormalities noted in the combined treatment groups were cerebral palsy (CP) in 6 children (4%); hypotonia (not with CP) in 28 (18%); hypertonia (not with CP) in 11 (7%); focal abnormalities (not with CP) in 5 (3%); and abnormalities of special senses in 2 (1%).

Scores on the Psychomotor Development Index (PDI) (motor function) of the Bayley Scales were lower among infants randomized to CA ( $p = .003$ ). Similarly, longer duration of CA was associated with lower PDI score ( $p = .01$ ). Scores on the Mental Development Index (precursors of cognitive function) tended to be lower in the CA group ( $p = .06$ ). However, the duration of CA was not significantly associated with MDI score. The score on the Pagan Test of Infant Intelligence was not related to support method.

Abnormalities on MR were not associated with treatment assignment or with duration of CA. In the combined treatment groups, 11 (8%) had possible abnormalities and 22 (15%) had definite

abnormalities. The most common specific abnormalities included ventricular dilation (20. 14%) and infarction (13, 9%).

In multivariate analyses, EEC seizure activity in the first 48 hours postoperatively was associated with lower PDI scores ( $p = .001$ ) and greater risk of MR abnormalities ( $p < .001$ ).

In summary, longer duration of CA is associated with a greater likelihood of abnormal neurologic examination and worse motor function at age one year, although early cognitive function was not affected. Furthermore, postoperative EEG seizure activity is an independent predictor of poor motor function and structural brain abnormalities on MR. The significance of these findings for longer-term neurologic outcome awaits follow-up of the study cohort at age 4 years.

\*By invitation

### 3. MICROEMBOLI DURING CABG. GENESIS AND EFFECT ON OUTCOME

Richard E. Clark, M.D., Donalee A. Davis, C.N.R.N.\*, Mark R. Lovell, Ph.D.\*,

George J. Magovern, M.D. and Jon Brillman, M.D.\*

*Pittsburgh, Pennsylvania*

The hypothesis tested in this prospective clinical study was that microemboli (ME) generation were both a function of cardiopulmonary bypass and the operation and that outcomes were related to total number of microemboli. One hundred eleven patients having CABG had continuous transcranial Doppler (TCD) recordings of middle cerebral artery flow made from the time of induction to transfer to the ICU using a 2 Mz transducer. ME were recorded as clear unambiguous instantaneous perturbations of the velocity signa. Correlations of ME to surgical intervals were made: pre-cannulation, aortotomy, insertion and removal of the aortic cannula, vent, and cardioplegia needle, aortic cross-clamping (total and partial) and clamp removal, defibrillation, displacement of the heart and other maneuvers. Pre- and post-cognitive neuropsychologic (NP) testing was performed in 25 patients for orientation, attention, comprehension, repetitive, naming constructional ability, memory, calculation, and reasoning similarities and judgement. The total ME during CPBP were correlated with post-operative encephalopathy, CVA and cardiopulmonary complications. Analysis of variance for repeated measures, chi square (Pearson, Mental-Hacngel, and Fisher's) and correlations by Pearson's and Spearman's methods were made.

There was a mean of  $32 \pm 3$  ME per patient detected. CPBP contributed approximately 10-20% of the total ME/pt. Aortic cannulation, aortic clamp removal (total and partial) and especially cardiac displacement contributed most of the ME. All phases of the NP test were slightly depressed ( $< 0.03$ ) in the immediate post-operative interval. The most striking were language comprehension ( $p < 0.003$ ), language repetition ( $p < 0.002$ ), constructional ability ( $p < 0.016$ ), and reasoning judgement ( $0.01$ ). Total ME were only related to decreases in language repetition ( $p < 0.02$ ).

ME total counts  $> 65$  were related to post-operative encephalopathy, CVA, and cardiopulmonary complications ( $p = 0.02$ ) as 10 of 13 patients had one of these complications. These data show that the initial hypothesis that CPBP was a major contributor of ME was incorrect. ME were markedly reduced during aortic cannulation by use of a dry air-filled cannula as opposed to a fluid-filled one. A greater number of cases are now performed under a single cross-clamping and repeated lifting of the heart to inspect posterior anastomoses is avoided whenever possible. Further, high numbers of ME (2 x mean) or  $> 65$  increase risk of encephalopathy CVA and cardiopulmonary complications by at least 20% above that expected. It is concluded that non-

invasive TCD studies of a middle cerebral artery velocity have been useful in determining etiology and possible remedial measures for reduction in CNS complications after operations.

**9:45 a.m. INTERMISSION - VISIT EXHIBITS**

\*By invitation

**10:30 a.m. SCIENTIFIC SESSION - Grand Ballroom**

**Moderators: Robert B. Wallace, M.D.**

**James L. Cox, M.D.**

**4. CARDIAC TRANSPLANT VASCULOPATHY: A MULTI-VARIABLE ANALYSIS OF DISEASE DEVELOPMENT AND MORBID EVENTS**

David C. McGiffin\*, Timo Savunen, M.D.\*, James K. Kirklin, M.D., David C. Naftel, Ph.D.\*, Robert C. Bourge, M.D.\*, Connie White-Williams, R.N.\* and Tero Sisto, M.D.\*

*Birmingham, Alabama*

Coronary artery disease (CAD) after cardiac transplantation (C Tx) is possibly the major obstacle to long-term survival, yet limited information is available about the determinants and patterns of disease progression and risk factors for serious coronary events. The development and progression of CAD after C Tx was analyzed in 217 consecutive patients (pts) undergoing C Tx between 1981 and December 1990 with followup through 6/30/92. Post C Tx coronary angiograms (angios) (n=632 in 157 pts) were reviewed and scored according to location and extent of CAD. The actuarial freedom from any CAD (by angio) was 81% at 2 yrs., 47% at 5 yrs, and 20% at 8 yrs post C Tx. Males developed CAD more often than females (30% vs 50% free of CAD at 5 yrs.,  $p=.01$ ). By multivariable analysis, risk factors identified for CAD included recipient pre-Tx positive CMV serology ( $p=.002$ ) and older donor age ( $p=.07$ ). Progression of CAD was compared among pts with early vs. later onset of CAD (by angio); there was no difference in average CAD progression among pts who developed disease in first 2 yrs vs those with CAD-free (angio) interval of 3-6 yrs ( $p=.4$ ). Serious coronary events (CE) [CAD severe enough for retransplantation (re-Tx) (n=8) and/or death from CAD (n=9)] occurred in 15 pts, of which 4 underwent re-Tx. The actuarial freedom from CE was 88% at 5 yrs and 79% at 8 yrs. By multivariable analysis, only race mismatch ( $p=.03$ ) and male recipient ( $p=.07$ ) were risk factors for CE. The rate of CAD progression was greater in the group who suffered CE vs those who did not ( $p<.0001$ ), but 6 of the 15 pts (40%) with CE died suddenly with severe CAD without angio evidence of CAD a mean of 13 months before death.

Inferences:

- \* CAD by angio exists in >80% of late C Tx survivors by 8 years, and the incidence is greater among recipients with positive CMV serology and older donor hearts.
- \* Once identified, the rate of angiographic CAD progression is similar regardless of the prior disease-free interval.
- \* Despite the frequency of CAD, serious coronary events (relisting for re-Tx or CAD death) occur in only about 20% of pts by 8 yrs, and are more likely among male recipients and with donor/recipient race mismatch.
- \* Despite routine yearly surveillance angios, about 40% of coronary events present as sudden death without evident CAD.

\*By invitation

## 5. PULMONARY BIPARTITION WITH BILATERAL LOBAR TRANSPLANTATION: A NEW APPROACH TO ORGAN SHORTAGE

Jean-Paul J. Couetil, M.D.\*, Antoine Achkar, M.D.\*, Christian R. Brizard, M.D.\*,  
Peter L. Birnbaum, M.D.\*, Alain Guinvarch, M.D.\*, Jean-Philippe Kieffer, M.D.\*,  
Didier F. Loulmet, M.D.\*, Catherine I. Amrein, M.D.\*, Remain J. Guillemain, M.D.\*,  
Patrick Chevalier, M.D.\*, John Y.M. Relland, M.D.\*, Jacques Rochemaure, M.D.\*  
and Alain F. Carpentier, M.D., Ph.D.

*Paris, France*

The scarcity of small donors has significantly limited lung transplantation (LTx) for pediatric and small adult patients. Lobectomy of grafts procured from size unmatched donors overcame this difficulty but only in a few selected cases; in addition, it represented a waste of lung tissue. In our research laboratory, we have shown that it is possible to divide one lung with careful partition of the vascular and bronchial structures in order to obtain two viable lobar grafts suitable for a bilateral LTx in a smaller animal. In this paper, we report our clinical experience of a bilateral Tx using the donor left lung in 3 patients with an average weight of 44 kg. The indications were idiopathic pulmonary fibrosis, cystic fibrosis (CF) and emphysema. The CF patient received in addition to the BLTx a reduced-size liver transplant for associated end-stage liver failure. Recipients (R) and donors (D) characteristics are given in the following table.

	R1/D1	R2/D2	R3/D3
Age	42/20	17/25	44/17
Weight (kg)	40/80	36/69	56/100
Height (cm)	150/80	154/174	158/190
TLC (liter)	4.10/3.26**	4.01/3.04*	5.57/3.66*

\* TLC: Total Lung Capacity. Predicted TLC has been calculated using the European Community for Coal and Steel formula.

\*\* Predicted value of left lung as 45% of calculated TLC of the donor

The surgical technique consists of a careful partitioning of the left donor lung, a bilateral anterior thoracotomy of the recipient, and, under cardio-pulmonary bypass, the implantation of the lower lobe in the left hemithorax and the upper lobe in the right hemithorax. Vascular and bronchial connections are facilitated by leaving a long pedicle on the recipient side. The pulmonary artery anastomosis for the donor left upper lobe is performed with the "fissure side" of the artery to ensure an anastomosis without torsion. An end to end bronchial anastomosis overcomes the problem of size discrepancy.

All 3 patients are alive and well 1 to 6 months after the operation. All were discharged from the hospital within the first or second postoperative month. No technical problems were identified. Repeated bronchoscopy has demonstrated satisfactory healing without early stricture formation. All patients demonstrated normal room air arterial blood gases postoperatively. Forced expiratory

volume l/sec has shown progressive improvement with all patients achieving 75% of predicted values. A perfect adaptation of the transplanted lobes to the recipient pleural space was demonstrated by postoperative CT scan.

In conclusion, bilateral lobar transplantation is possible in hypotrophic adults or children with large size discrepancy from the donor lung. It may help resolve the problem of donor availability in the pediatric population. Further experience and follow-up are needed to define the indications and the possible limitations of this procedure.

**11:15 a.m. PRESIDENTIAL ADDRESS**

**The Education of a Cardiothoracic Surgeon:**

**An Appollonian Quest**

Aldo R.Castaneda, M.D., Boston, Massachusetts

**12:00 p.m. ADJOURN FOR LUNCH IN EXHIBIT HALL - VISIT EXHIBITS**

\*By invitation

**MONDAY AFTERNOON, APRIL 25, 1994**

**1:30 p.m. SCIENTIFIC SESSION - Grand Ballroom**

**Moderators: William A. Gay, Jr., M.D.**

**Valerie W. Rusch, M.D.**

**6. AN INSTITUTIONAL STUDY OF IMPROVING OUTCOMES AFTER THE**

**ARTERIAL SWITCH OPERATION**

Gil Wernovsky, M.D.\*, John E. Mayer, Jr., M.D., Richard A. Jonas, M.D., John W. Kirklin, M.D., Eugene H. Blackstone, M.D., Frank L. Hanley, M.D. and Aldo R. Castaneda, M.D., Ph.D.

*Boston, Massachusetts; Birmingham, Alabama and San Francisco, California*

30 hospital deaths and 10 late deaths occurred among 470 patients undergoing an arterial switch operation in one institution between January 1983 and January 1992. The ventricular septum was essentially intact in 278, and a VSD (with double outlet ventricle in 28) was repaired in the other 192. A proper cross-sectional followup was performed in 1992. Multivariable analysis (hazard function domain) showed earlier date of operation to be a risk factor for death but only in the case of the senior surgeon ( $P < .0001$  for interaction term  $< .0001$ ); three new surgeons had survivals as high as the senior surgeon and no date of operation effect (Figure).

There were no clusters of deaths. Other multivariably determined patient risk factors for death were 1) retropulmonary course of left main or circumflex coronary artery, in various patterns, 2) dextrocardia, 3) older age at operation (Figure).



Procedural risk factors included 1) longer duration of circulatory arrest (linear relation, 3% deaths after 15 minutes, 14% after 90 minutes,  $P=.006$ ), 2) concomitant aortic arch augmentation. The early improvement was related to overall improvements, not to neutralization of any one risk factor (although the duration of circulatory arrest was inversely related to date of operation,  $r=.4$ ,  $P<.0001$ ); improvement occurred along with reduction from 20% (1985) to 2.4% (1990, 1991) of patients in whom the arterial switch was aborted to an atrial switch. 61 patients underwent reintervention, usually (40 patients) for right ventricular outflow obstruction and within the first year after operation; the prevalence is less in recent years ( $P>=.0002$ ). 98% of surviving patients are functionally normal at last followup.

\*By invitation

## 7. LEFT VENTRICULAR FUNCTION EVALUATION UP TO FIVE YEARS AFTER DYNAMIC CARDIOMYOPLASTY

Luiz F.P. Moreira, M.D.\*, Noedir A.G. Stolf, M.D.\*, Edimar A. Bocchi, M.D.\*, Paulo M.P. Fernandes, M.D.\*, Fernando Bacal, M.D.\* and Adib D. Jatene, M.D.

### *Sao Paulo, Brazil*

Improvement of left ventricular function after dynamic cardiomyoplasty has been reported in patients with severe cardiomyopathies, but the long-term effects of this procedure remain unclear. In this study, 30 patients submitted to cardiomyoplasty for treatment of dilated cardiomyopathy were annually investigated with radionuclide scintigraphy, Doppler-echocardiography and right heart catheterization. They were in NYHA functional class III or IV before operation. There were no operative deaths and patients were followed-up from 3 to 66 months (mean, 24 months). Eleven patients died and one patient was submitted to heart transplantation during late follow up. Actuarial survival rates were 83.9% at 1 year, 66.2% at 2 years and 41% at 5 years of follow-up. Multivariate analysis of factors influencing outcome documented that long-term survival was significantly affected by preoperative functional class and pulmonary vascular resistance. Otherwise, NYHA functional class improved from  $3.2 \pm 0.4$  to  $1.6 \pm 0.6$  in the surviving patients ( $p<0.01$ ). Furthermore, sequential laboratory investigation showed the long-term cardiomyoplasty influence on LV ejection fraction (LVEF), cardiac index (CI), LV stroke index (LVSI), pulmonary wedge pressure (PWP) and LV stroke work index (LVSWI): (\* =  $p<0.05$ , in relation to preoperative data)

(Pts)	Preop.(25)	6 Mo.(25)	1 Yr.(19)	2Yr.(11)	3 Yr.(7)	4 Yr.(6)	5 Yr.(4)
LVEF (%)	20 ± 3	24 ± 6*	23 ± 6*	24 ± 6*	23 ± 3	21 ± 3	20 ± 4
CI (l/min/m <sup>2</sup> )	1.9 ± 0.3	2 ± 0.4	2 ± 0.4	2 ± 0.3	2.2 ± 0.3	2.2 ± 0.3	2.2 ± 0.2
LVSI (ml/m <sup>2</sup> )	21 ± 3	25 ± 7 *	24 ± 7*	25 ± 5 *	29 ± 4*	27 ± 6*	27 ± 5
PWP (mmHg)	24 ± 6	19 ± 6*	18 ± 6*	18 ± 7*	14 ± 3*	16 ± 6	19 ± 7
LVSWI (g.m/m <sup>2</sup> )	18 ± 5	26 ± 9*	25 ± 9*	25 ± 7*	33 ± 10*	29 ± 10*	27 ± 9

Thus, despite the LVEF tendency to decrease at late cardiomyoplasty follow-up, the long-term course of patients with dilated cardiomyopathy submitted to this procedure seems to be characterized by the maintenance of hemodynamic improvement. Otherwise, long-term survival after cardiomyoplasty is limited by the severity of patients' compromise before the operation.

\*By invitation

## **8. INCIDENCE OF LOCAL RECURRENCE AND SECOND PRIMARY TUMORS IN RESECTED STAGE I LUNG CANCER**

Nael Martini, M.D., Manjit S. Bains, M.D., Michael E. Burt, M.D., Ph.D., Maureen F. Zakowski, M.D.\*, Patricia McCormack, M.D., Valerie W. Rusch, M.D. and Robert J. Ginsberg, M.D.

*New York, New York*

From 1973 to 1985, 598 patients underwent resection for stage I non-small cell lung cancer. There were 291 T1 lesions and 307 T2. The male to female ration was 1.9:1. The histology was squamous carcinoma in 233 and non-squamous carcinoma in 365. Lobectomy was performed in 511 patients (85%), pneumonectomy in 25 (4%), and wedge resection or segmentectomy in 62 (11%). A mediastinal lymph node dissection was carried out in 560 patients (94%) and no lymph node dissection in 38 (6%). There were 14 post-operative deaths (2.3%).

Ninety-nine percent of the patients were followed for a minimum of 5 years or until death with an overall median follow up of 86 months. The overall five and ten-year survivals (Kaplan-Meier) were 75% and 66%. Survival in T1N0 tumors was (82%) at 5 years and 73% at 10 years compared to 68% at 5 years and 60% at 10 years for T2 tumors (p=0.009).

The overall incidence of recurrence was 27% (local or regional 26%. systemic 74%) and was not influenced by histology. There were 204 patients who developed second primary cancers (34%). Of these, 69 (34%) were second primary lung cancers.

Despite complete resection. 31 of 62 patients (50%) who had wedge resection or segmentectomy had recurrence. Five and 10 year survivals following wedge resection or segmentectomy were 59% and 35% significantly less than those undergoing lobectomy. The 5 and 10 year survivals in the 38 patients who had no lymph node dissection was also reduced to 59% and 32% respectively.

Apart from the favorable prognosis observed in this group of patients, three facts emerge as significant: 1) the importance of systematic lymph node dissection to ensure that these patients have truly stage I disease; 2) lesser resections (wedge/segment) result in high recurrence rates and reduced survival regardless of histology; and 3) the incidence of 2nd primary lung cancers is high in the long-term survivors.

### **2:30 p.m. BASIC SCIENCE LECTURE**

#### **Traffic Signals for Leukocyte Emigration from the Blood Stream**

Timothy A. Springer, Ph.D., Boston, Massachusetts

### **3:15 p.m. INTERMISSION - VISIT EXHIBITS**

\*By invitation

### **4:00 p.m. SCIENTIFIC SESSION - Grand Ballroom**

**Moderators: Bruce A. Reitz, M.D.**

**L. Penfield Faber, M.D**

## 9. COX-MAZE PROCEDURE FOR CHRONIC ATRIAL FIBRILLATION ASSOCIATED WITH MITRAL VALVE DISEASE

Yoshio Kosakai, M.D.\*, Akira T. Kawaguchi, M.D.\*, Fumitaka Isobe, M.D.\*,  
Yoshikado Sasako, M.D.\*, Yoshitsugu Kito, M.D.\* and Yasunaru Kawashima, M.D.  
*Osaka, Japan*

Atrial fibrillation (AF) often persists even after a successful mitral operation, undermining hemodynamics and necessitating anticoagulation. To treat AF associated with mitral valve disease, we combined Cox-Maze procedure in 62 patients with AF undergoing mitral valve repair (n=28) or replacement (n=34), including 16 reoperated cases. Associated procedures included aortic valve operation (22), tricuspid annuloplasty (32), atrial plication (10) and others (3). Duration of AF varied from 0.1 to 23 (average  $8.3 \pm 6.4$ ) years, the f-wave voltage ranged from 0 to 0.45 ( $0.16 \pm 0.09$ ) mV, and cardiothoracic ratio varied from 46 to 85 ( $64 \pm 9$ ) %. We used separate atriotomies and cryoablation to preserve the sinus node artery. The superior vena cava was transected to improve exposure of the mitral valve. Aortic cross-clamp time varied from 92 to 212 ( $142 \pm 25$ ) minutes with bypass time ranging from 148 to 295 ( $226 \pm 33$ ) minutes. There were no early or late deaths in the follow-up ranging from 0.2 to 18.9 ( $7.8 \pm 5.0$ ) months. Although 3 patients required pacemaker implantation for sinus node dysfunction, a regular sinus or atrial rhythm was restored in 92% (46/50), 91% (31/34), and 100% (15/15) of patients 3, 6, and 12 months after surgery. The atrial a-wave was detected in 97% in the trans-tricuspid flow and 73% in the trans-mitral flow. Twenty-one patients are free from anti-arrhythmics, and all 11 patients with an atrial a-wave and a repaired valve are off anticoagulation 3 months after surgery. Since no preoperative variables are indicative of postoperative AF, Cox-Maze procedure is indicated to all patients with chronic AF undergoing mitral valve operation.

\*By invitation

## 10. REPAIR OF THE AORTIC VALVE IN PATIENTS WITH AORTIC INSUFFICIENCY AND AORTIC ROOT ANEURYSM

Tirone E. David, M.D., Joanne Bos, R.N.\* and Christopher M. Feindel, M.D.\*  
*Toronto, Ontario, Canada*

Composite replacement of the aortic valve (AV) and ascending aorta is the standard operation for pts with aortic insufficiency (AI) and aortic root aneurysm. However, the AV can be repaired in approximately one-third of these pts because the AV leaflets are normal or minimally diseased. The AI is due to annuloaortic ectasia and/or increase in the diameter of the sinotubular junction. When annuloaortic ectasia is marked, an aortic annuloplasty with reimplantation of the AV in a tubular Dacron graft is performed ("Reimplantation"). When annuloaortic ectasia is mild or absent, replacement of the sinuses of Valsalva and ascending aorta with a tailored tubular Dacron graft of diameter 10% smaller than the diameter of the aortic annulus is performed ("Remodelling"). In both types of procedures the coronary arteries have to be reimplanted into the Dacron graft.

From July 1989 to September 1993, 40 pts with AI and aortic root aneurysm had surgery with preservation of the AV. The pts clinical profile was the following.

	Reimplantation	Remodelling
Number of pts	19	21
Age (range) - years	44 (14 to 68)	65 (32 to 76)
Aortic root size (mm)	$56 \pm 5$	$61 \pm 8$
AI (grades 0 to 4)	$2.8 \pm 0.8$	$2.7 \pm 0.9$

Marfan syndrome	10	2
Acute type A dissection	8	1
Mitral regurgitation	3	0
Coronary artery disease	1	3

There was no operative death but one pt (the 2nd of the "reimplantation" series) had persistent AI and required composite replacement of the AV and ascending aorta. All pts have been followed from 1 to 52 months, mean of 19. A 14 year-old pt with Marfan syndrome required AVR two years later because of AI due to marked increase in the size of the leaflets. The remaining 38 pts have stable AV repair and have not had any cardiovascular complication. No one has more than mild AI as assessed by periodical Doppler echocardiographic studies.

These two types of AV repair have provided excellent clinical results in adult pts with AI and aortic root aneurysm, and the function of the AV has remained stable up to 52 months postoperatively.

\*By invitation

## 11. LOBECTOMY: VATS VS THORACOTOMY. A RANDOMIZED STUDY

Thomas J. Kirby, M.D.\*, Michael Mack, M.D.\*, Rodney Landreneau, M.D.\* and Thomas W. Rice, M.D.

*Cleveland, Ohio; Dallas, Texas and Pittsburgh, Pennsylvania*

The exact rose of video-assisted thoracic surgery (VATS) remains to be clearly defined by randomized studies comparing VATS to accepted thoracic surgical techniques and approaches. VATS lobectomy was compared to open thoracotomy in 55 patients randomized to either a muscle sparing thoracotomy (MST) and lobectomy (30 patients) or a VATS lobectomy (25 patients). All patients were carefully staged preoperatively and intraoperatively and found to have stage I or II non-small cell lung carcinoma. Each patient underwent a complete and potentially curative anatomic lobectomy using accepted thoracic surgical and oncologic principles. The two groups were compared using operating room time, intraoperative and postoperative complications, length of chest tube drainage, hospital stay and number of days of parenteral narcotics. The results are shown below.

	Age	Op Time (min)	CT (days)	LOS (days)	ParNar
<b>MST</b>	61.4	175 ± 85	5.1 ± 2.8	7.7 ± 5.6	3.8 ± 2.1
<b>VATS</b>	58.7	141 ± 70	4.4 ± 3.5	6.3 ± 3.4	2.6 ± 1.5

(Op Time-operating room time, CT-length of chest tube drainage, LOS= length of hospital stay, ParNar-Days of parenteral narcotics)

There was no significant difference between the two groups in operating room time, length of chest tube drainage, hospital stay or length of parenteral narcotic use. No significant intraoperative complications occurred in the VATS group requiring emergent conversion to a thoracotomy or intraoperative blood transfusion. Four VATS lobectomies were converted to a MST for technical reasons.

We conclude that VATS lobectomy does not offer significant advantages over a muscle sparing thoracotomy while in our opinion exposing the patient to the as yet undefined risk of performing a major pulmonary resection in an essentially closed chest.

\*By invitation

## **12. THIRTEEN YEAR EXPERIENCE WITH "HOMOVITAL" HOMOGRAFTS FOR AORTIC VALVE REPLACEMENT**

Magdi H. Yacoub, F.R.C.S., Nasser R.H. Rasmi, M.D.\*, Thoralf M. Sundt, M.D.\*, Eileen Boyland,\*, Asghar Khaghani, F.R.C.S.\*, Rosemary C. Radley-Smith, F.R.C.P., F.A.C.C.\* and Andrew G. Mitchell, F.R.C.P.\*

### ***Harefield, England***

Between February 1980 and July 1993, 264 patients have undergone aortic valve replacement using homografts taken under sterile conditions from patients undergoing cardiac transplantation and preserved at 4°C in tissue culture medium (mean interval = 3.9 days). Patients ranged in age from 1.5 to 79 years (mean = 45.5, SD = 19.4). The underlying pathology was congenital in 100 (76 bicuspid valves), calcific in 50, rheumatic in 30, Marfan syndrome in 9, degenerative in 9 and malfunction of a previously replaced valve in 54. Twenty patients (7.6%) had bacterial endocarditis, 15 active of which 8 had underlying pathology. Freehand two suture line technique was used in 144 and aortic root replacement with reimplantation of the coronaries in 120. Associated procedures were performed in 94 patients. The operative mortality was 3.4% for the total group of patients (264) and 0.6% mortality in the isolated group (170). With a mean follow up period of 4.1 years (SD = 3.4), there was 4.5% late mortality for the total group. Actuarial survival at 5 and 10 years for the entire group was 92.8%, 90.2% and was 95.7%, 92.0% for those undergoing isolated valve replacement. Seven patients have required reoperation for valve failure (1.5 to 8.2 years postoperative), 5 due to bacterial endocarditis (3 recurrent and 2 de novo); 1 due to valve degeneration and 1 due to technical failure, with no mortalities. The probability of freedom from valve failure was 97.8% and 91.2% at 5 and 10 years in the entire group of patients. There have been no episodes of thromboembolism. Thus far, multivariant analysis did not identify any risk factor for late degeneration including ABO incompatibility (known in all patients) and HLA matching (known in 37). We conclude that homovital homograft valves provide good 10 year results without evidence of accelerated rejection.

\*By invitation

## **TUESDAY MORNING, APRIL 26, 1994**

### **7:00 a.m. FORUM SESSION I - Grand Ballroom**

**Moderators: Andrew S. Wechsler, M.D.**

**Richard D. Weisel, M.D.**

### **F1. MOLECULAR CARDIOMYOPLASTY - CARDIAC GENE THERAPY**

Stanley K.C. Tarn, M.D.\*, Wei Gu, Ph.D.\* and Bernardo Nadal-Ginard, M.D., Ph.D.\*

*Cambridge and Boston, Massachusetts*

Cardiomyoplasty, an operation consisting of synchronously paced skeletal muscle, commonly the latissimus dorsi, wrapped around the heart, offers a potential treatment of chronic heart failure, by using the power derived from skeletal muscle. Another strategy to treat heart failure is to provide additional endogenous power, i.e. more cardiac myocytes. Cardiac myocytes become terminally differentiated and lose their ability to undergo mitosis soon after the newborn period. As yet, no cardiac myogenic transcription factor has been identified. However, skeletal myogenic factors, the MyoD family of basic helix-loop-helix proteins, have been well-described. Studies have demonstrated that these basic helix-loop-helix proteins can function as master genes for induction of the skeletal muscle expression program, i.e. transfection of the MyoD gene has been shown to mediate the conversion of mouse C3H10T1/2 fibroblasts into stable myoblasts, which could be

induced to undergo terminal differentiation into myotubes. Since essentially the same structural contractile apparatus is shared by both cardiac and skeletal myocytes, conversion of cardiac fibroblasts, for example those in a scar following myocardial infarction, into potentially functional skeletal myocytes may be of benefit for the treatment of heart failure. Sense and anti-sense MyoD genes were cloned into retroviral vectors carrying G418 resistance. Primary cardiac fibroblasts, freshly isolated from newborn rats, were infected with virus carrying sense or anti-sense MyoD gene. Ten days post-infection and post-G418 selection, expression of MyoD protein was demonstrated in 95% of cells infected with sense MyoD virus by intense nuclear immunostaining, using a MyoD polyclonal antibody. In contrast, none of the cells infected with anti-sense MyoD virus showed staining. Upon withdrawal of growth factors, 95% of MyoD positive cells became elongated and, in the presence of appropriate cell density, fused to form multi-nucleated cells, morphologically similar to striated muscle cell. Spontaneous contractile movements were noted in 10% of the cells. Expression of a myogenic differentiation marker, myosin heavy chain, in 95% of these elongated cells were detected by intense cytoplasmic immunostaining, using a myosin heavy chain monoclonal antibody. In contrast, MyoD negative cells remained unchanged. In summary, cardiac fibroblasts were able to be converted into bona fide potentially functional skeletal myocytes as shown by definitive morphologic and biochemical changes. Further studies are needed to explore this unique strategy to treat heart failure.

\*By invitation

## **F2. NITROGLYCERIN MAINTAINS GRAFT VASCULAR HOMEOSTASIS AND ENHANCES PRESERVATION IN AN ORTHOTOPIC RAT LUNG TRANSPLANT MODEL**

Yoshifumi Naka, M.D., Ph.D.\*, Nepal C. Chowdhury, M.D.\*, Mehmet C. Oz, M.D.\*<sup>t</sup>,

Robert E. Michler, M.D.\*, Osvaldo J. Yano, M.D.\*, Craig R. Smith, M.D., David M.

Stern, M.D.\* and David J. Pinsky, M.D.\*

*New York, New York*

Pulmonary dysfunction following lung transplantation often occurs for poorly understood reasons. Because our pilot studies show that endothelial cells exposed to hypoxia and reoxygenation have undetectable nitric oxide (NO) levels due to the quenching effect of oxygen free radicals, and NO is vasodilatory, antithrombotic and prevents neutrophil adherence, we hypothesized that the NO donor nitroglycerin (NTG) might enhance lung preservation for transplantation. We used a new orthotopic rat lung transplant model in which the native PA is ligated so that hemodynamic assessment and survival depends exclusively upon the transplanted lung. The left lung was harvested from 22 rats in double blinded experiments, flushed (pressure < 20 mm Hg) with either lactated Ringer's (LR, n=11) or LR+NTG 0.1mg/ml (LR+NTG, n=11), preserved for 4 hrs at 4°C, followed by orthotopic transplantation. Baseline measurements immediately upon reperfusion included arterial pO<sub>2</sub> (mm Hg), pulmonary artery flow (PAF, ml/min), mean PA pressure (MPAP, mm Hg), and left atrial pressure (LAP, mm Hg). After ligation of the right PA, these measurements were recorded simultaneously every 5 min for 30 minutes or until recipient death, after which myeloperoxidase assays (MPO,  $\uparrow$ ABS<sub>460</sub> nm/min) were performed to quantify neutrophil deposition. Pulmonary vascular resistance (PVR, Woods units x 1000) was calculated as (MPAP-LAP)/PAF. After 4 hrs preservation, 0% of the LR rats survived 30 min, whereas 64%

of the NTG rats survived ( $p < 0.01$ ). Hemodynamic measurements ( $\pm$  SEM) recorded at the final time at which the recipient was alive are shown below ( $*=p < 0.05$ ).

	PAF	MPAP	PVR	pO <sub>2</sub>	MPO
LR	0.4 $\pm$ 0.1	10.5 $\pm$ 0.7	5.7 $\pm$ 2.1	130 $\pm$ 39	2.6 $\pm$ 0.3
LR+NTG	6.4 $\pm$ 2.2*	17.4 $\pm$ 3.0*	1.1 $\pm$ 0.2*	339 $\pm$ 66*	1.7 $\pm$ 0.3*

In similar experiments, nitroglycerin also significantly lengthens the effective preservation offered by Euro-Collins to over 8 hours. Supplementation of preservation solutions with NTG enhances blood flow, reduces PVR, diminishes leukostasis in the transplanted lung, and improves recipient survival. Nitroglycerin may be beneficial in clinical lung transplantation.

†1994-96 Research Scholar

\*By invitation

### F3. IMMEDIATE EARLY GENE EXPRESSION IN HUMAN SAPHENOUS VEINS HARVESTED DURING CORONARY ARTERY BYPASS SURGERY

Richard A. Moggio, M.D., Jia-Zhen Ding, M.D.\*, Carolyn J. Smith, Ph.D.\*, Robert R. Tota, M.D.\*, Michael B. Stemmerman, M.D.\* and George E. Reed, M.D.

*Valhalla, New York*

Saphenous vein graft (SVG) occlusion is a common late complication of coronary bypass (CABG). Intimal smooth muscle cell hyperplasia (SMC) is a component of this pathobiology, but the underlying molecular events are poorly understood. Immediate early genes (IEG) are activated shortly after growth stimulation and subserve cellular functions which may contribute to intimal SMC accumulation. In the present study, human SVG were harvested with minimal manipulation during CABG and processed for isolation of total RNA to examine changes in IEG mRNA expression by Northern blotting techniques. Thirty SVG were incubated at 4°C in Dulbecco's Modified Eagle media from 30 minutes to 6 hours. The mRNAs for c-fos and c-myc were weak or undetectable in controls, but were increased (>10 times controls) within one hour (c-fos), and persisted for at least 6 hours (c-myc) after harvest. c-fos is a transcription factor which can activate genes that affect cell growth and differentiation, c-myc regulates proliferation in various cell types. Anti-sense oligonucleotides have targeted c-myc mRNA and related IEGs, and have been shown to prevent intimal SMC hyperplasia in animal models of vascular injury.

Our results demonstrate, for the first time in human vascular tissue, incipient IEG induction. This information may lead to molecular therapies to control SVG disease, restenosis following angioplasty and atherosclerosis in general.

\*By invitation

### F4. GENE THERAPY USING ADENOVIRAL VECTOR TRANSFER OF THE HSV-THYMIDINE KINASE GENE AS AN APPROACH FOR TREATMENT OF HUMAN MALIGNANT MESOTHELIOMA

W. Roy Smythe, M.D.\*, Harry C. Hwang, B.A.\*, Kunjlata M. Amin, Ph.D.\*, James

M. Wilson, M.D., Ph.D.\*, Steven M. Albelda, M.D.\* and Larry R. Kaiser, M.D.

*Philadelphia, Pennsylvania*

Malignant pleural mesothelioma is a neoplasm that is unresponsive to conventional cell and tissue-level toxic chemotherapies, however, gene therapy offers potential to treat such tumors at a subcellular level with minimal toxicity to normal cells. Cells expressing the herpes simplex thymidine kinase gene (HSVtk) may be killed when exposed to ganciclovir (GCV) due to production of a toxic nucleotide analog that interferes with cell replication. We theorized that recombinant adenoviral vectors could transfer HSVtk to mesothelioma and effect cell killing both *in vitro* and *in vivo* after exposure to GCV.

Two human malignant mesothelioma cell lines were infected by adenovirus vectors carrying a Rous Sarcoma Virus promoter and either the HSVtk gene (Ad.RSV.tk) or a non-therapeutic marker gene (Ad.RSV.lacZ - gene for  $\beta$ -galactosidase) at a multiplicity of infection of 100 viral particles/cell. Cells were then exposed to varying concentrations of GCV in media for 4 days, with viable cell growth assessed by colorimetric assay. GCV sensitivity, expressed concentration necessary to eliminate 50% of viable cells (IC50) is shown below.

**Table 1. Mesothelioma / GCV IC50**

Cell Type	AdRSVtk	AdRSVlacZ	uninfected
1-45	<0.1 $\mu$ M	> 1000 $\mu$ M	>750 $\mu$ M
REN	< 1.0 $\mu$ M	> 1000 $\mu$ M	>1000 $\mu$ M

$2 \times 10^7$  1-45 cells infected *in vitro* with either Ad.RSV.tk or Ad.RSV.lacZ were then injected into subcutaneous flank tissues (R=lacZ, L=HSVtk) of three Severe Combined Immune Deficient mice. After three days, animals had developed bilateral tumors of 6-8 mm diameter and began treatment with 5 mg of intraperitoneal GCV/day. By day ten, left flank tumors in all animals (HSVtk side) were undetectable, with continued growth of tumors derived from Ad.RSV.lacZ infected cells.

In conclusion, we demonstrate that recombinant adenoviral vectors can transfer a therapeutic HSVtk prodrug gene to human mesothelioma, effecting substantial acute *in vitro* cellular killing and complete *in vivo* tumor regression with exposure to non toxic doses of the drug GCV.

\*By invitation

**F5. INTRAUTERINE CREATION OF INCREASED PULMONARY BLOOD FLOW IN LAMBS: POSTNATAL PULMONARY HYPERTENSION AND EARLY PULMONARY ENDOTHELIAL DYSFUNCTION**

V. Mohan Reddy, M.D.\*, Jackson Wong, M.D.\*, John L. Liddicoat, M.D.\*, Frank L. Hanley, M.D.\* and Jeffrey R. Fineman, M.D.\*

*San Francisco, California*

*Sponsored by: Benson B. Roe, M.D., San Francisco, California*

Pulmonary hypertension is a common accompaniment of congenital heart disease with increased pulmonary blood flow, and remains a major source of morbidity and mortality in the peri- and post-operative period. Previous models developed to study this problem have entailed placement of aorta to pulmonary shunts postnatally; after pulmonary vascular resistance has fallen and a period of lung growth and development has occurred. To establish a model which mimics the clinical setting of increased pulmonary blood flow during the transition circulation and immediately



after birth, we placed gore-tex vascular grafts between the aorta and main pulmonary artery in 8 late gestation fetal sheep.

Recent evidence suggests that endothelial injury secondary to increased pulmonary blood flow disrupts the normal regulatory mechanisms provided by the vascular endothelial cells, and may contribute to the development of pulmonary hypertension and increased vascular reactivity. To investigate this hypothesis, the responses to ATP (an endothelium-dependent vasodilator), sodium nitroprusside (SNP, an endothelium-independent vasodilator), endothelin-1 (ET-1, a vasoactive polypeptide produced by vascular endothelium), and alveolar hypoxia (8.0% oxygen) in these shunted lambs (at 4 weeks of age) were compared to historical (1-2 week old) controls.

Six fetuses had 4.0-6.0 mm grafts placed between the bovine trunk and the main pulmonary artery. Four weeks after spontaneous delivery, mean pulmonary arterial pressure (PAP) was  $24.7 \pm 3.9$  mmHg (controls =  $13.0 \pm 3.0$  mmHg). The ratio of PAP to systemic arterial pressure (SAP) was  $0.27 \pm 0.09$ . The ratio of pulmonary to systemic blood flow (Qp/Qs) was  $2.1:1 \pm 0.7$ . Two fetuses had an 8.0 mm graft placed between the ascending aorta and the main pulmonary artery. At 4 weeks of age, PAP was  $58.5 \pm 7.7$  mmHg, PAP/SAP was  $0.95 \pm 0.05$ , Qp/Qs was  $1.6:1 \pm 0.2$ , and pulmonary vascular resistance was  $3.1 \pm 0.3$  mmHg min<sup>-1</sup>kg L<sup>-1</sup>(control = 0.65). The percent changes in PAP in response to the vasoactive stimuli are shown in the table below.

	PERCENT CHANGE IN PAP			
	ATP	SNP	ET-1	HYPOXIA
SHUNTED	-0.9% ± 1.9*	-29.9% ± 8.8	+31.8% ± 14.4*	+60.4% ± 32.7*
CONTROLS	-24.7% ± 2.5†	-33.5% ± 15.4†	-24.1% ± 7.5†	+35.6% ± 17.3

\* p<0.05, vs. Controls Value by the unpaired t-test

† Value obtained during pulmonary hypertension induced by U46619 (a thromboxane A<sub>2</sub> mimic).

This preparation is the first model of pulmonary hypertension secondary to congenital increased pulmonary blood flow, and is a useful tool to study the development of pulmonary hypertension and increased vascular reactivity secondary to congenital heart disease. Increased pulmonary blood flow produces early selective endothelial dysfunction (as manifested by impaired endothelium-dependent vasodilation and ET-1-induced vasoconstriction) and increased vascular reactivity to hypoxia. A better understanding of the development of pulmonary hypertension secondary to congenital heart disease will optimize the timing of surgical repair and improve the peri- and postoperative management.

\*By invitation

## F6. MARKED ENHANCEMENT IN MYOCARDIAL FUNCTION RESULTING FROM OVEREXPRESSION OF A HUMAN P-ADRENERGIC RECEPTOR GENE

Carmelo A. Milano, M.D.\*, Lee F. Allen, M.D., Ph.D.\*, Paul C. Dolbert, Ph.D.\*, David Johnson, Ph.D.\*, Howard A. Rockman, M.D.\*, Richard Bond, Ph.D.\* and Robert J. Lefkowitz, M.D.\*

*Durham, North Carolina and Houston, Texas*

Molecular biological approaches have affected significant advances in the understanding and treatment of disease; however, it has been difficult to apply this technology to the study of myocardial function. Using transgenic animals, this study examines whether overexpression of a  $\beta_2$ -adrenergic receptor ( $\beta_2$ -ADR) gene can improve baseline myocardial function.

Transgenic mice were created using a fusion gene composed of the coding sequence for the human  $\beta_2$ -ADR flanked at its 5' end by the alpha-myosin heavy chain promoter-enhancer sequence. Northern blot analysis of total RNA from six muscle containing tissues demonstrated intense,

cardiac specific expression. Three lines of transgenic mice overexpressing the receptor were established. Radioligand binding assays performed on myocardial membrane fractions from the line with highest expression, quantitated total  $\beta^2$ -ADR as  $35.4 \pm 13.3$  pmol/mg protein in the transgenics vs.  $0.2 \pm 0.09$  pmol/mg in controls (n=4; 175 fold increase). Immunohistochemical staining with a human  $\beta^2$ -ADR specific antibody revealed receptor protein expression on the sarcolemma in all four cardiac chambers. Adenylyl cyclase activity was determined by incubating membrane fractions with [ $^{32}$ P]-ATP and quantitating the rate of [ $^{32}$ P]-cAMP formation. In four independent experiments, both basal and isoproterenol stimulated cyclase activity were increased in the transgenics vs. paired littermate controls: basal -  $290 \pm 104$  pmol/min/mg protein vs.  $160 \pm 27$  (p<0.05, paired T-test); isoproterenol stimulated -  $495 \pm 123$  vs.  $356 \pm 112$  (p<0.05). In addition, the isoproterenol dose response curve was shifted markedly to the left in the transgenics relative to controls, indicating greater isoproterenol sensitivity. Myocardial function was assessed first in the atrial tissue where gene expression was greatest; isometric tension development was measured in both right and left atria hung in organ perfusion baths. To simulate *in vivo* conditions, right atria were allowed to contract at their intrinsic rate, and left atria were paced at the rate of their corresponding right atrium; basal and maximal isoproterenol-stimulated tensions were recorded. Comparing 6 transgenic right atria to 7 controls, basal transgenic tension was increased  $170.8 \pm 24.9$  mg vs.  $104.2 \pm 16.2$ , (p<0.05, student's T-test). Comparing 5 transgenic left atria to 8 controls, basal transgenic tension was increased 3 fold:  $239 \pm 49.3$  mg vs.  $81.9 \pm 24.1$  (p<0.005). In addition, basal left atrial tension in transgenics equaled or exceeded maximally stimulated tension in the controls:  $239 \pm 49.8$  mg vs.  $173.1 \pm 13$  (p=0.143). Histologic examination of the hearts of 2 month old animals with collagen-specific stains demonstrated no changes in collagen content relative to controls; there was no evidence of fibrosis or myocyte necrosis. Heart/body weight ratios were not statistically different in the transgenics relative to nontransgenic littermate controls (n=6 pairs).

In conclusion, the alpha-myosin heavy chain promoter-enhancer sequence affects intense cardiac specific gene expression. Overexpression of ( $\beta^2$ -ADRs results in a marked enhancement of both basal biochemical and physiologic parameters of myocardial function. The intrinsic myocardial dysfunction and reduced  $\beta^2$ -ADR-mediated adenylyl cyclase activity common to many forms of heart failure, suggest a potential therapeutic role for ( $\beta^2$ -ADR Overexpression. As methods for *in vivo* gene transfer develop, targeted Overexpression of specific genes in the myocardium may serve as an important adjunct to current surgical or medical treatments.

\*By invitation

## **F7. RETROGRADE CEREBRAL PERFUSION FOR DISLODGE MENT OF SOLID CEREBRAL EMBOLI**

Alon S. Aharon, M.D.\*, Hillel Laks, M.D., Jeffrey Pearl, M.D.\*, Ehud Rudis, M.D.\*,

Lester Permut, M.D.\*, John Frazee, M.D.\*, Eli Ziv, B.S.\*, Gary Mathern, M.D.\*,

Anthony Verity, M.D.\*, Davis Drinkwater, M.D.\*, Eli Kaczer, B.S.\* and Paul Chang,

B.S.\*

*Los Angeles, California*

A primate model was created in order to investigate the efficacy of retro-perfusing ischemic brain following embolization of atherosclerotic debris during cardiac surgery. Retrograde cerebral perfusion via the superior vena cava (SVC) with oxygenated whole blood and moderate

hypothermia was used as a method of washing out embolized atherosclerotic plaque and supporting ischemic brain in the baboon. Animals were divided into a control group (n=4) which underwent selective internal carotid artery (ICA) embolization of atherosclerotic plaque and a treated group (n=4) which underwent selective ICA embolization followed by cerebral retroperfusion via the SVC. Animals were anesthetized with Forane inhalation anesthetic and paralyzed with a non-depolarizing agent. Cardiopulmonary bypass (CPB) at blood flows of  $100 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  and mean arterial pressure above 70 mm Hg was initiated with bicaval cannulation and moderate systemic hypothermia to 28 degrees C. Both groups underwent cold blood cardioplegic arrest and selective ICA embolization using 10 mg of human atherosclerotic debris ranging in size from 250 to 500 microns. Following embolization control animals were rewarmed and weaned from CPB. Experimental animals underwent an additional 5 minute period of cerebral retroperfusion via the SVC with cold oxygenated blood at a mean perfusion pressure of 40 mm Hg before rewarming and weaning from CPB. Fourteen channel electroencephalogram (EEG) performed immediately after termination of CPB revealed signs of severe central nervous system (CNS) injury in all control animals which included: non reactive backgrounds signifying brain death in 3 of 4 animals, persistent lateralizing epileptiform discharges in 3 of 4 animals and lateralized findings in 4 of 4 animals. In the retroperfusion group post-CPB EEG revealed no evidence of significant CNS injury and all animals remained cortically reactive. Somatosensory evoked potentials (SSEP) using bilateral median nerve stimulation obtained in the last 5 animals revealed loss of thalamo-cortical peaks in 3 of 3 control animals and retention of thalamo-cortical peaks in 2 of 2 retroperfused animals. SSEP demonstrated a decrease in cortical reactivity 10-45 minutes after embolization in all animals with large areas of cerebral infarction. Microscopic analysis of formalin perfused fixed brains in animals sacrificed 36 to 48 hours after embolization revealed greater volumes of infarction in control animals when compared to animals treated with retroperfusion (1% vs. 5% via planimetry, 1% vs. 6% via computer digital analysis). Conclusions: (1) SSEP monitoring appears to correlate with early CNS injury and may be a valuable monitoring technique and (2) cerebral retroperfusion performed during CPB with moderate hypothermia can prevent or decrease the extent of CNS ischemic injury seen after embolization of atherosclerotic debris which may be an important cause of stroke after cardiac surgery.

\*By invitation

## **F8. PLATELET FACTOR 4 - AN ALTERNATIVE TO PROTAMINE**

Alvise F. Bernabei, M.D.\*, Nicolas Gikakis\*, Theodore E. Malone, Ph.D.\*, Stefan Niewiarowski, M.D., Ph.D.\* and L. Henry Edmunds, Jr., M.D.

*Detroit, Michigan; Philadelphia, Pennsylvania and Cambridge, Massachusetts*

Protamine sulfate (PS), used to inhibit heparin, often causes adverse reactions after cardiopulmonary bypass (CPB). Platelet factor 4 (PF4), a natural protein stored in platelet alpha granules, inhibits heparin. We compared the efficacy, safety and side effects of recombinant PF4 (rPF4) and PS inhibition of heparin in nine young female adult baboons (12-18 kg) with and without CPB.

In 12 trials each anesthetized, intubated baboon received 100 units/kg heparin IV; after 5-10 minutes, heparin was completely neutralized by bolus injection of 1 mgm/kg PS or 2 mgm/kg rPF4. Mean arterial, pulmonary arterial and pulmonary capillary wedge pressure decreased significantly ( $p>0.05$ ) after PS only.

In 13 more trials, each baboon received 300 units/kg heparin and was perfused for 30 minutes at 50 ml/kg/min from right atrium to femoral artery using 8-10 Fr polyurethane cannulas, a roller

pump, and an 0.8 M2 spiral coil oxygenator. Following decannulation, either 3 mgm/kg protamine or 6 mgm/kg rPF4 was injected. Neither drug caused significant ( $p>0.05$ ) change in mean arterial, pulmonary arterial, central venous or wedge pressures or in cardiac output (thermodilution) 5 and 30 minutes after drug injection. Thrombin time and partial thromboplastin time remained significantly prolonged five minutes after injection of protamine, but returned to baseline at 30 minutes; both times were normal five minutes after rPF4. In contrast to rPF4, PS had an anticoagulant effect at high concentrations. After both drugs, template bleeding times were prolonged. Platelet count and responses to ADP did not differ between drugs. rPF4 increased activated complement 3 (C3a) from  $91.3 \pm 7.7$  ng/ml to  $150 \pm 3.5$  at 5 min; protamine increased C3a from  $72 \pm 4.2$  to  $99.4 \pm 5.5$  ( $p<0.05$ , between groups). All animals remain healthy.

We conclude that rPF4 neutralizes heparin faster than PS and has no anticoagulant effect at high concentration. Both drugs activate complement, but in baboons the small increases are unimportant. Neither drug causes adverse side effects in baboons. The data support a decision for a clinical trial of rPF4.

\*By invitation

### F9. THE NOVEL EFFECTS OF 3, 5, 3' TRIIODOTHYRONINE UPON MYOCYTE CONTRACTILE FUNCTION AND (3-ADRENERGIC RESPONSIVENESS IN DILATED CARDIOMYOPATHY

Jennifer D. Walker, M.D.\*, Francis G. Spinale, M.D., Ph.D.\*, Rupak Mukherjee, M.S.\* and Fred A. Crawford, Jr., M.D.

*Charleston, South Carolina*

The number of patients undergoing cardiac surgery with chronic left ventricular (LV) dysfunction is increasing. These patients frequently require intensive inotropic support in the perioperative period. Recent clinical and experimental studies have suggested that 3, 5, 3' triiodothyronine ( $T_3$ ) improves LV pump function. However, whether  $T_3$  directly improves myocyte contractile function in cardiomyopathic disease is unknown. Accordingly, this study examined the direct effects of  $T_3$  upon isolated myocyte contractile function in cells obtained from control ( $n=6$ ) pigs and pigs with tachycardia induced dilated cardiomyopathy (DCM; atrial pacing at 240 bpm for 3 weeks;  $n=6$ ). Myocyte percent shortening (MYO-%) and myocyte velocity of shortening (MYO-VEL  $\mu\text{m/s}$ ) were obtained at baseline and in the presence of  $T_3$  (1-100 pM  $T_3$ ). (\* $p<0.05$  vs baseline, #  $p<0.05$  vs control myocytes)

	Baseline		80pM $T_3$		100pM $T_3$	
	MYO-%	MYO-VEL	MYO-%	MYO-VEL	MYO-%	MYO-VEL
Control ( $n=30$ )	4.4 $\pm$ 0.1	43.8 $\pm$ 1.5	6.0 $\pm$ 0.3*	58.9 $\pm$ 3.6*	6.1 $\pm$ 0.3*	69.9 $\pm$ 3.7*
DCM( $n=14$ )	2.1 $\pm$ 0.1	26.7 $\pm$ 1.3	2.5 $\pm$ 0.1*#	39.9 $\pm$ 5.6*#	2.8 $\pm$ 0.5*#	44.1 $\pm$ 102*#

For both control and DCM groups,  $T_3$  (80 and 100  $\mu\text{M}$ ) caused a significant increase in myocyte contractile function. Clinically, a common method of inotropic support is stimulation of the (3-adrenergic receptor system (PAR). Accordingly, a second series of experiments was performed in which control and DCM myocyte contractile function was examined with the ( $\beta^2$ AR agonist, isoproterenol (ISO=25nM) alone, and in myocytes preincubated with 80 and 100 pM  $T_3$  to which isoproterenol was added. (+ $p<0.05$  vs ISO)

Isoproterenol	80pM $T_3$ + ISO	100pM $T_3$ + ISO
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	<u>MYO-%</u>	<u>MYO-VEL</u>	<u>MYO-%</u>	<u>MYO-VEL</u>	<u>MYO-%</u>	<u>MYO-VEL</u>
Control (n=30)	8.8±0.7	100.2±1.5	11.3±0.7+	152.9±11.0+	11.8±0.6+	155.1±8.5+
DCM(n=14)	4.9±0.5	73.7±9.1	5.6±0.9+	129.3±28.5+	5.7±1.4+	116.8±29.8+

For both the control and DCM groups, myocyte contractile function increased with preincubation of T<sub>3</sub> over isoproterenol values alone. Further, MYO-VEL increased by over 300% in DCM myocytes following preincubation with 100 pM T<sub>3</sub> followed by ISO compared to a 200% increase in control myocytes (p<0.05). The results from this study clearly demonstrated that T<sub>3</sub> directly augments myocyte contractile function in both control and DCM myocytes. In addition, T<sub>3</sub> significantly enhanced myocyte contractile function following Î²AR stimulation in cardiomyopathic myocytes. This study provides unique evidence to suggest that T<sub>3</sub> may be a useful adjunct to conventional inotropic support in the setting of advanced left ventricular dysfunction.

\*By invitation

## 9:00 a.m. SCIENTIFIC SESSIONS - Grand Ballroom

**Moderators: Delos M. Cosgrove, M.D.**

**Douglas J. Mathisen, M.D.**

### 13. INTERMEDIATE RESULTS FOLLOWING COMPLETE REPAIR OF TETRALOGY OF FALLOT IN NEONATES

Hani A. Hennein, M.D.\*, Ralph S. Mosca, M.D.\*, Gonzalo Urcelay, M.D.\*, Dennis

C. Crowley, M.D.\* and Edward L. Bove, M.D.

*Ann Arbor, Michigan*

From July 1988 through September 1993, 30 neonates with symptomatic tetralogy of Fallot (TOP) underwent complete repair. Sixteen patients had uncomplicated TOP, 9 had TOP and pulmonary atresia (PA), 3 had TOP with nonconfluent pulmonary arteries (NCPA), and 2 had TOP, PA and NCPA. The median age at operation was 11 days (mean ± SEM, 12.6 ± 2.9 days) with a mean weight of 3.1 ± 0.1 kg (range, 1.5 - 4.4 kg). Preoperatively, 14 patients were receiving an infusion of prostaglandin, 13 were mechanically ventilated, and 6 required inotropic support. Right ventricular outflow obstruction (RVOTO) was managed by a limited transannular patch in 25 patients, infundibular muscle division with limited resection in 15, and insertion of an RV-PA valved aortic homograft conduit in 5 patients. Follow up was complete at a median interval of 24 months (range, 1-62 months). There were no hospital deaths and two late deaths resulting in one month, one year and five year actuarial survival rates of 100%, 93% and 93%, respectively. The hazard function for death had a rapidly declining single phase that approached zero by 6 months after surgery. Both deaths occurred in patients with TOP/PA who had undergone aortic homograft conduit RVOT reconstruction, making the only independent risk factor for death the use of a valved aortic homograft conduit (p<0.005). Eight patients required reoperation, resulting in one month, one year and five year freedom from reoperation rates of 100%, 93% and 66%, respectively. Indications for reoperation were branch left pulmonary artery stenosis in 5 patients, RVOTO in 2 patients, and severe pulmonary insufficiency in 1 patient. Independent risk factors for reoperation included an intraoperative RV/LV pressure ratio of 0.75 or greater (p=0.04), Doppler residual left pulmonary artery stenosis of ≥15 mmHg, or Doppler RVOT gradient of ≥40 mmHg at hospital discharge (p=0.002 and 0.02, respectively). This series demonstrates the safety of early complete repair of symptomatic tetralogy of Fallot in neonates. It also emphasizes the importance of relieving

all sources of RVOTO at the initial operation, particularly that located at the ductus insertion site, which may be difficult to diagnose in the neonate before ductal closure occurs. The safety and efficacy of valved aortic homograft conduits in neonates requires further investigation.

\*By invitation

#### 14. OPTIMIZING SELECTION OF PATIENTS FOR MAJOR LUNG RESECTION

Mark K. Ferguson, M.D.†, Laurie B. Reeder, M.D.\* and Rosemarie Mick, M.S.\*

*Chicago, Illinois*

**Background:** Diffusing capacity (DLCO) correlates with mortality and pulmonary morbidity following lung resection. It is not known whether a normal DLCO permits safe resection in patients with marginal spirometric values, or whether normal spirometric values negate the adverse effects of a low DLCO. The purposes of this study were: 1) to determine the best predictors of morbidity and mortality; and 2) to assess whether interactions exist between DLCO and spirometry that help estimate outcome after major lung resection.

**Methods:** We performed a retrospective analysis of 376 patients who underwent lung resection from 1980 to 1992 (222 men, 154 women; mean age 60.1 years). 307 had lung cancer (Stage I:127; II:55; IIIa:120) and 69 had other disease. 284 underwent lobectomy/bilobectomy and 92 had pneumonectomy. We assessed the relationship of 21 preoperative variables to 20 postoperative events classified as pulmonary (PULM) or (CARD) complications, overall nonfatal morbidity (MORE), and operative mortality (MORT).

**Results:** The best single predictor of complications was the predicted postoperative DLCO (ppoDLCO%; calculated by multiplying the percentage of unresected lung segments by the measured preoperative DLCO expressed as a percent of predicted;  $p < .004$  for each outcome by univariate analysis). The incidence of complications was inversely related to ppoDLCO% (Cochran-Armitage trend test):

		ppoDLCO%†	<40	40-50	50-60	60-70	>70	p
Incidence (%)	PULM	(53/279)	33.3	16.7	32.7	16.9	8.3	.001
	CARD	(52/260)	31.2	27.3	19.1	18.5	14.9	.005
	MORB	(121/270)	55.9	47.1	61.5	35.5	36.3	.003
	MORT	(19/289)	19.4	13.2	5.3	1.6	3.1	.0003

Stepwise logistic regression analysis based on 9 significant variables (age, sex, NYHA class, prior MI, FVC%, DLCO%, FEV<sub>1</sub>%, ppoFEV<sub>1</sub>%, ppoDLCO%) identified only ppoDLCO% and age as predictors of PULM, MORB and MORT, and these with prior MI predicted CARD (model significance  $p < .001$  by  $\chi^2$  for each complication). There was no interaction between spirometry and ppoDLCO% in predicting complications. Eliminating patients with ppoDLCO% <50 theoretically would have reduced the mortality by >50% (from 6.5% to 3.2%).

**Conclusion:** DLCO measures subtle but important changes in lung function that often are undetected by spirometry. It independently and strongly predicts the risk of complications and mortality following lung resection, and its routine use is invaluable in the preoperative assessment of lung resection candidates.

†1986-88 Research Scholar

\*By invitation

**15. ESTIMATION OF PATIENT-SPECIFIC RISK OF PROSTHETIC VALVE REOPERATION WITH REFERENCE TO PROPHYLACTIC VALVE REPLACEMENT**

Jeffrey M. Piehler, M.D., Eugene H. Blackstone, M.D., Kent R. Bailey, Ph.D.\*, Michael E. Sullivan, M.D.\*, James R. Pluth, M.D, Noel S. Weiss, M.D, Dr.P.H.\* and Ronald S. Brookmeyer, Ph.D.\*

*Kansas City, Missouri; Birmingham, Alabama; Rochester, Minnesota; Portland, Oregon; Scottsdale, Arizona; Seattle, Washington and Baltimore, Maryland*

One of the major variables in the decision to prophylactically replace a prosthetic heart valve is a patient-specific estimate of operative risk. To date no study has provided the means to make this estimation for both low and high risk subgroups. Consequently, a cooperative review of 2246 prosthetic valve reoperations performed between 1963 and 1992 at three experienced academic institutions was undertaken. The records were subjected to multivariable logistic regression analyses of 53 variables with potential influence upon hospital mortality. Those variables which would be known preoperatively and which were found to have the strongest correlation with mortality (Table) were incorporated into a predictive risk equation which was internally validated. Predicted risks varied widely from less than 1% to greater than 99%. No institutional or temporal risk factors were identified.

<b><u>Incremental Risk Factor</u></b>	<b><u>p-value</u></b>
Demographic	
Age	<.0001
Weight	.0008
Left Ventricular Function and Secondary Conditions	
NYHA Class (I-V)	<.0001
Hemodynamic Status	<.0001
Tricuspid Incompetance	<.0001
Extensiveness of Valvular Heart Disease	
Multiple Valve Disease	.002
Previous Cardiac Surgery	
Number of Previous Open Heart Operations	.001
Coexisting Morbid Conditions	
Prosthetic Valve Endocarditis	<.0001
Renal Failure	.01
Concomitant Procedures	
Repair of Ascending Aortic Aneurysm	<.0001
Coronary Artery Bypass Grafting	.009
Left Ventricular Aneurysmectomy	.005

With limits placed upon contributing risk factors, the predictive risk equation can be utilized to construct nomograms for estimating operative risk (Figure). Nevertheless, solving

the equation for an individual patient is relatively straightforward and markedly more specific. For example, estimated risk of a first elective single valve reoperation in a 55-year old woman who is NYHA Class I, without coexisting morbid conditions or concomitant procedures is only 1.5% (90% confidence limits 1.2%-1.9%). In contrast, estimated risk for the same operation in a 68-year old woman, Class III, with elevated creatinine, tricuspid incompetence, and the need for coronary bypass is 43% (33%-54%). We conclude that hospital mortality for prosthetic valve reoperation can be accurately predicted and is generally low for most uncomplicated patients. Such data has applicability to analysis of prophylactic valve replacement and other clinical situations.

\*By invitation

#### **10:45 a.m. SCIENTIFIC SESSION - Grand Ballroom**

**Moderators: Aldo R. Castaneda, M.D.**

**James L. Cox, M.D.**

#### **16. FACTORS ASSOCIATED WITH EARLY AND LATE RISK AFTER FONTAN OPERATIONS**

John E. Mayer, Jr., M.D., Thomas Gentles, M.D.\*, John Kupferschmid, M.D.\*, Gil

Wernovsky, M.D.\*, Richard A. Jonas, M.D. and Aldo R. Castaneda, M.D., Ph.D.

*Boston, Massachusetts*

Early survival after Fontan operations for functional single ventricle (including tricuspid atresia) show continued improvement despite expanded selection criteria. Few reports provide information on factors influencing longer term outcome. Among 500 consecutive Fontan operations (1973-1991) 82 early and 36 late failures (death, transplant or takedown) occurred. In 1992-93 we obtained follow-up on 392 of the 418 early survivors. Separate analyses were carried out for early and late failure. Univariate analysis identified potentially risk factors ( $p > 0.1$ ) which were entered into logistic regression analyses. Risk factors for early failure (all with  $p < 0.05$ ) were age  $< 4$  yrs, any history of PA hypertension, presence of a common AV valve, aortic saturation  $< 80\%$ , PA pressure  $> 15$  mmHg, pulmonary arteriolar resistance  $> 2$  Wood units, pulmonary artery distortion, tricuspid valve as the systemic AV valve, and use of right atrial appendage or free wall in Fontan pathway. Fenestration reduced early risk. However, the only risk factors for late failure were atriopulmonary (vs cavopulmonary) anastomoses, presence of a pacemaker, and aortic cross clamp time  $> 55$  minutes. The late survival curve shows a continuing risk out to at least 15 years. Thus, once patients survive the Fontan operation, morphologic and physiologic characteristics have little impact on late survival, but surgical technique variables continue to exert an effect.

\*By invitation

#### **17. HEMODYNAMIC AND PHYSIOLOGIC CHANGES DURING IMPLANTABLE LVAD SUPPORT**

Patrick M. McCarthy, M.D.\*, Karen B. James, M.D.\*, Emmanuel L. Bravo, M.D.\*, Robert M. Savage, M.D.\*, Rita Vargo, R.N.\*, Shelly K. Sapp, M.S.\*, Marlene Goormastic, M.P.H.\* and James D. Thomas, M.D.\*



Cleveland, Ohio

Sponsored by: Delos M. Cosgrove, M.D., Cleveland, Ohio

To evaluate hemodynamic effectiveness and changes in patient (pt) physiology on the HeartMate® left ventricular assist device (LVAD), we studied 19 moribund bridge to heart transplant pts (35 to 62 years old, mean 50 years). All pts were on inotropes pre-LVAD, 16 (84%) were on a balloon pump, and 3 (16%) were on heparin-coated ECMO for circulatory support. Three pts died, all had right ventricular (RV) dysfunction and developed multiple organ failure. Three pts are rehabilitated and are awaiting a donor. Of the 16 survivors (84%), 13 have been transplanted (Tx), and post-Tx survival is 100%. Duration of LVAD support averaged 66 days (22 to 101 days). Pts on support over 30 days were NYHA class I before Tx. There were no thromboembolic events with over 1100 patient days of support. Only aspirin and persantine were administered. Significant hemodynamic improvement occurred:

	Pre-LVAD (n=19) (mean ± SD)	Pre-Tx (n=13) (mean ± SD)	p value
Cardiac index (L/inin/m <sup>2</sup> )	1.6 ± 0.2	3.2* ± 0.9	.0002
Left atrial pressure (mmHg)	22.9 ± 9.5	8.0 ± 5.5	.034
RV ejection fraction	19.8 ± 11.3	40.8 ± 8.9	.005
Pulmonary vascular resistance (Wood units)	5.2 ± 2.6	2.0 ± 0.8	.0001

\* mean "pump index during support

Bilirubin, blood urea nitrogen, plasma renin activity, angiotensin II, arginine vasopressin, plasma epinephrine, and plasma norepinephrine all decreased to normal, or near-normal, pre-Tx (all values p<.001 percent change from baseline pre-LVAD). Atrial natriuretic peptide levels decreased (326 ± 301 pg/ml to 185 ± 89 pg/ml) but did not return to normal (26-33 pg/ml).

We conclude that: 1) implantable LVAD support improved hemodynamic function in 84% of pts; 2) NYHA class improved, as well as subsystem function and the neurohormonal axis; 3) chronic LVAD support with a low risk of thromboemboli is attainable.

\*By invitation

**11:25 a.m. ADDRESS BY HONORED SPEAKER**

A Thoracic Tale of Two Cities

Rodolfo Herrera-Llerandi, M.D., Guatemala City, Guatemala

**12:10 p.m. ADJOURN FOR LUNCH IN EXHIBIT HALL - VISIT EXHIBITS**

**12:10 p.m. CARDIOTHORACIC RESIDENTS' LUNCHEON -**

**Petite Trianon**

## TUESDAY AFTERNOON, APRIL 26, 1994

### 1:45 p.m. SIMULTANEOUS SCIENTIFIC SESSION A - ADULT CARDIAC SURGERY

**East Ballroom**

**Moderators: John L. Ochsner, M.D.**

**Tirone E. David, M.D.**

#### **18. LONG TERM RESULTS OF VALVE REPLACEMENT WITH THE ST. JUDE MEDICAL PROSTHESIS**

Eugene M. Baudet, M.D.\*, Vincent Fuel, M.D.\*, Francois Roques, M.D.\*, Frederic Clerc, M.D.\*, Xavier Roques, M.D.\* and Nadine Laborde, M.D.\*

*Bordeaux, France*

*Sponsored by: D. Craig Miller, M.D., Stanford, California*

Since June 12, 1978, the St. Jude Medical (SJM) valve has been routinely used as our mechanical prosthesis of choice; through September, 1993, 2,714 SJM valves were implanted. To assess results with truly long follow-up, we reviewed the first 1,112 patients (pts) undergoing 1,244 valve replacements with the SJM prosthesis before June 12, 1987: Aortic (AYR) = 773 pts (69%), Mitral (MVR) = 207 pts (19%) or Mitral and Aortic position (DVR) = 132 pts (12%). The mean patient age was 55.9 years (range 9 months to 82 yrs) and 690 pts (62%) were males. There were 42 hospital deaths (3.8%). Follow-up was 98% complete (8,988 pt-yrs), with a mean of 9.75 yrs, range 6-15 yrs. There were 213 late deaths: 91 or 43% (60 AYR, 19 MVR, 12 DVR) were considered valve-related. Eleven (12%) were due to prosthetic valve endocarditis (PVE), 27 (30%) to sudden death (SD), 9 (10%) to valve thrombosis (VT), 19 (21%) to thromboembolism (TE), 22 (24%) to anticoagulant-related hemorrhage (ACRH), and 3 (3%) to paravalvular leak (PVL). Actuarial survival, at 14 yrs, including hospital mortality, was  $69 \pm 7\%$  for AVR,  $68 \pm 11\%$  for MVR and  $59 \pm 16\%$  for DVR. Linearized rates of late valve-related events included: TE (1.09% pt-yr), ACRH (0.94% pt-yr), PVE (0.32% pt-yr), VT (0.33% pt-yr), PVL (0.34% pt-yr). Actuarial freedom, at 14 yrs, from TE was  $89 \pm 3\%$ , ACRH ( $83 \pm 8\%$ ), VT ( $97 \pm 1\%$ ), reoperation ( $95 \pm 3\%$ ). Long term actuarial freedom from all valve-related deaths was  $84 \pm 6\%$ , and  $61 \pm 8\%$  from all valve-related morbidity and mortality. At follow-up, 93% of the survivors were in NYHA class I or II.

With one of the longest follow-up experiences reported for this prosthesis, the St. Jude valve has proven, because of its low thrombogenicity, low incidence of valve-related events, and low valve-related mortality, to be one of the best performing mechanical prosthesis currently available. Nevertheless, the late valve-related complications and deaths illustrate how our quest for a "perfect" prosthesis still remains unfulfilled.

\*By invitation

## 19. THE CARPENTIER-EDWARDS PERICARDIAL AORTIC VALVE; TEN YEAR RESULTS

Delos M. Cosgrove, M.D., Bruce W. Lytle, M.D.\*, Paul C. Taylor, M.D.\*, Margarita T. Camacho, M.D.\*, Robert W. Stewart, M.D.\*, Patrick M. McCarthy, M.D.\* and Floyd D. Loop, M.D.  
*Cleveland, Ohio*

The utilization of bioprostheses in the aortic position has been limited by the restrictive hemodynamics and suboptimal durability of porcine valves. Pericardial valves solved the hemodynamic problems but most pericardial valve designs demonstrate an unacceptably high rate of structural valve deterioration. To evaluate the function of the Carpentier-Edwards pericardial valve in aortic position the results of 310 aortic valve replacements performed between 1982 and 1985 were analyzed. Mean age was  $64.2 \pm 10.8$  years (range 22-95); 190 (61.3%) were males. Isolated aortic valve replacement was performed in 272 patients (87.7%). There were 18 hospital deaths (5.8%) and none were valve related.

Follow up of the 292 survivors was 100% complete at a mean of  $8.8 \pm 0.8$  years; 2, 209 patient years of follow up were available for analyses. There were 119 (40.7%) late deaths. Actuarial survival at 5 and 10 years were 82.5% and 55.2% respectively.

	10 year actuarial	
	<u>freedom from events</u> (%)	<u>Linearized rate</u> (%/pt year)
Thromboembolism	88.5 $\pm$ 2.2	1.6 $\pm$ 5.0
Hemorrhage	90.4 $\pm$ 1.8	1.0 $\pm$ 3.7
Endocarditis	94.2 $\pm$ 1.6	0.7 $\pm$ 3.2
Structural deterioration	88.2 $\pm$ 3.6	0.6 $\pm$ 2.8

The 153 patients  $\geq 65$  had an extremely low incidence of structural valve deterioration with only 4 explants and 95.1% actuarial freedom from explant at 10 years and a linearized rate of  $0.4 \pm 2.3\%$  per patient year compared to 83.5% and  $0.9 \pm 3.2$  for patients  $< 65$ .

Fourteen valves were explanted for structural deterioration. Of these 13 (93%) had leaflet calcification causing stenosis and one had a wear-related leaflet tear.

We conclude that the Carpentier-Edwards pericardial valve 1) has a low incidence of valve-related complications; 2) structural deterioration is infrequent and results from leaflet calcification. 3) The low incidence of structural deterioration in patients  $\geq 65$  makes this valve an increasingly appropriate option in this group.

\*By invitation

## 20. MID-TERM RESULTS OF AORTIC VALVE REPLACEMENT WITH STENTLESS PORCINE AORTIC VALVE

Christopher M. Feindel, M.D.\*, Tirone E. David, M.D., Joanne Bos, R.N.\*, Zhao Sun, M.A.\*, Susan Armstrong, MSc.\* and Hugh E. Scully, M.D.

*Toronto, Ontario, Canada*

A stentless porcine valve (SPV) has been used for aortic valve replacement (AYR) in 114 pts since 1987. There were 83 men and 31 women whose mean age was  $61 \pm 10$  years. Eleven pts were in chronic atrial fibrillation; 85 had aortic stenosis; 77 were in NYHA functional class 3 or 4, and 39 had coronary artery disease. The SPV was secured in the subcoronary position using the same

technique as for free-hand AY homograft. The mean SPV size was 26.4 mm (range 19 to 29 mm). There was only one operative death due to myocardial infarction but 6 pts had serious postoperative complications. Pts have been followed from 2 to 72 months, mean of 26. There have been 2 late deaths, neither one was valve-related. The actuarial survival at 5 years was 92% ± 3%. There have been only 3 valve-related complications: one infective endocarditis and two TIAs. Doppler echocardiographic studies have been performed annually; 89 pts have no AY insufficiency and 20 have mild. The mean AY area is 1.78 cm.sq. (range 1.1 to 3.0) and it has remained unchanged up to six years.

The SPV pts were individually matched with 376 pts who had AYR with Hancock II (HAN) bioprosthesis. The following variables were used for case-matching: age (±5 years), valve lesion, NYHA functional class, left ventricular ejection fraction (± 5%), and coronary artery disease (# of vessels diseased). Of 114 SPV pts, 101 were case-matched with 101 HAN pts. There was no operative mortality in matched pts. The actuarial survival at 5 years was 93% ± 4% for SPV pts and 86% ± 5% for HAN pts (p = ns). Proportional hazard analysis revealed that valve-related complications were three times more common in HAN pts than in SPV pts.

These data suggest that AYR with SVP is associated with a lower rate of valve-related complications than AYR with HAN. For this reason, AYR with SPV may enhance pts survival.

## **2:45 p.m. INTERMISSION - VISIT EXHIBITS**

\*By invitation

## **3:15 p.m. SIMULTANEOUS SCIENTIFIC SESSION A - ADULT CARDIAC SURGERY**

**East Ballroom**

**Moderators: John L. Ochsner, M.D.**

**Tirone E. David, M.D.**

### **21. RETROGRADE CARDIOPLEGIA DOES NOT PERFUSE THE RIGHT VENTRICLE**

Bradley S. Allen, M.D.\*, Renee S. Hartz, M.D., Jacqueline Wiewall, B.S.\*, Hanafy Hanafy, M.D.\*, Solomon Aronson, M.D.\*, Laurence Segil, M.D.\*, David Mayer, M.D.\*, Steven Feinstein, M.D.\*, Kirk Boiling, M.D., M.P.H.\* and Jongwok Ham, B.S.\*

*Chicago, Illinois*

Surgeons often rely primarily on retrograde cardioplegia for myocardial protection, since it provides adequate left ventricular (LV) perfusion, even in the presence of coronary artery disease. Clinically, however, adequate right ventricular (RV) perfusion by retrograde delivery, has not been demonstrated. Utilizing intraoperative TE echo, we examined retrograde delivery of cardioplegic solutions by contrast echocardiography which directly assesses myocardial perfusion. Fifteen patients (7CABG, SValves) had 4 cc's of sonicated Isovue® injected retrograde via a coronary sinus catheter. Quantitative assessment of myocardial perfusion was performed by visual inspection and background subtracted videodensitometric analysis. Prior to removing the aortic cross-clamp, myocardial oxygen extraction was calculated by first delivering 2 mins of warm blood cardioplegia retrograde, and then taking samples from the cardioplegic line and aortic root. This determined the oxygen extraction ratio across the myocardium at the end of retrograde delivery. Warm blood cardioplegia was next given

antegrade, and 15 sec's later samples taken from the cardioplegic line and a right ventricular (acute marginal) vein, to determine the oxygen extraction ratio across the RV. As assessed by contrast echo, retrograde infusion resulted in almost four times greater perfusion to the left ventricular free wall and septum, compared to the RV free wall (See graph).

Oxygen extraction across the myocardium supplied by retrograde infusion was low after two minutes. Conversely, when antegrade cardioplegia was started, R.V. oxygen extraction rose 4 fold ( $42 \pm 5\%$  vs  $11 \pm 1\%$ ,  $p < 0.05$ ) demonstrating that retrograde cardioplegia had not adequately perfused the RV myocardium.

Conclusions: 1. Retrograde cardioplegia provides poor R.V. myocardial perfusion as assessed by contrast echocardiography. (2) This poor perfusion is inadequate to meet myocardial demands as demonstrated by the high R.V. oxygen extraction after a prolonged retrograde infusion. (3) Therefore, surgeons must not rely solely on retrograde cardioplegia for RV myocardial protection. This concept is especially important if continuous warm blood cardioplegia is used, as myocardial requirements are then higher.

mean  $\pm$  S.E.

\*By invitation

## 22. THE CAPILLARY DISTRIBUTION OF RETROGRADE BLOOD CARDIOPLEGIA IN EXPLANTED HUMAN HEARTS

Abbas Ardehali, M.D.\*, Hillel Laks, M.D., Richard N. Gates, M.D.\*, Davis C. Drinkwater, M.D.\*, Thomas J. Sorensen, B.S.\* and Paul Chang, B.S.\*

*Los Angeles, California*

Warm retrograde blood cardioplegia (RBCP) for myocardial protection is frequently used despite several experimental animal studies questioning the adequacy of capillary flow to the right ventricle (RV) and septum. The capillary distribution of RBCP in the human heart is unknown. Hearts from 8 transplant recipients with the diagnosis of idiopathic/viral cardiomyopathy were arrested in situ with cold blood cardioplegia and excised with the coronary sinus intact. Within 20 minutes of explantation, colored microspheres ( $15 \pm 5 \mu\text{m}$ ) mixed in  $37^\circ\text{C}$  blood cardioplegia were administered through the coronary sinus at a pressure of 30-40 mm Hg for 2 minutes. Twelve transmural myocardial samples were taken horizontally at the level of midventricle and apex to determine regional capillary flow rates.

### **Results:**

Regional Capillary Flow Rates (cc/100gm/min)(Mean  $\pm$  SEM)

	RV	LV		Septum		Apex
Ant	<b>17.6 <math>\pm</math> 4.4</b>	46.4 $\pm$ 15.4	Ant	31.1 $\pm$ 10.1	LV	74.7 $\pm$ 21.9
Lat	<b>18.3 <math>\pm</math> 6.3</b>	49.3 $\pm$ 18.3	Mid	22.5 $\pm$ 5.4	RV	27.1 $\pm$ 5.9
Post	29.4 $\pm$ 15.1	76.1 $\pm$ 25.7	Post	24.3 $\pm$ 14.0	IVS	47.8 $\pm$ 10.2

At  $37^\circ\text{C}$ , approximately 18cc/100gm/min of capillary blood cardioplegia flow is needed to meet the metabolic requirements of the arrested human heart (Assuming a hemoglobin of 8 gm/dL, 100%  $\text{O}_2$  saturation, and 60%  $\text{O}_2$  extraction). Conclusions: In human hearts, RBCP delivered at a pressure of 30-40 mm Hg provides adequate capillary flow to the LV, septum, apex, and posterior

wall of RV. However, the capillary flow to the anterior and lateral wall of RV is marginal. These findings suggest that the RV of the human heart may not be adequately protected by warm RBCP.

\*By invitation

### 23. LONG-TERM FOLLOWUP OF 7551 CORONARY ARTERY BYPASS GRAFTS: FACTORS INFLUENCING PATENCY

William H. Coltharp, M.D.\*, Michael D. Decker, M.D.\*, William S. Stoney, M.D.,  
William C. Alford, Jr., M.D., George R. Burrus, M.D.\*, David M. Glassford, Jr.,  
M.D.\*, John W. Lea, IV, M.D.\*, Michael R. Petracek, M.D.\*, Todd A. Shuman,  
M.D.\* and Thomas D. Starkey, M.D.\*

#### *Nashville, Tennessee*

In order to assess the influence of patient characteristics (smoking history, diabetes mellitus, cholesterol history, age, sex, weight, and body surface area) and surgical technique (choice of conduit, choice of graft type, and vessel bypassed) on the long-term patency of coronary artery bypass (CAB) grafts, we evaluated surgical and catheterization data for 2317 patients who had at least one cardiac catheterization subsequent to coronary artery bypass. Duration of followup from CAB to last catheterization ranged from 7 days to 20.2 years (mean, 5.3 years) for the 7551 evaluable grafts. Graft patency was evaluated by Kaplan-Meier product-limit survivor analysis; cofactors were evaluated by Cox proportional hazards regression.

The overall graft patency rates were: 1 year, 96%; 2 years, 94%; 5 years 83%; 10 years 51%; 15 years 27%; and 20 years, 11%. These are conservative estimates, as they include only those patients who presented for repeat catheterization following CAB.

Patient characteristics that were significantly associated with duration of graft patency were sex, weight, and ever having smoked. Body surface area showed a significant association only when weight was not included in the model; history of diabetes was no longer significant once weight and sex were in the model.

Technical factors correlating significantly with graft survival were choice of conduit, graft type, and vessel bypassed. Graft patency rates were best for the anterior descending (AD) artery; intermediate for the acute marginal, circumflex, diagonal, obtuse marginal, posterior descending, posterior ventricular, right main and intermediate arteries; and least satisfactory for the left main and septal perforator arteries (patency rates at 10 years, 65%, 45% and 33% respectively; see Table). Internal mammary artery (IMA) grafts were associated with significantly better patency rates than were greater saphenous vein (GSV) grafts, an effect only partially explained by their more frequent use for AD grafts. Ten year survival rates were 53% for single grafts, 49% for sequential grafts, 47% for natural "Y" grafts, and 26% for constructed "Y" grafts.

	Conduit			Graft Type				Vessel Grafted		
	Left IMA	Right IMA	CSV	Single	Sequential	Natural Y	Constructed Y	AD	Middle Group	Inferior Group
5-year	90%	88%	83%	84%	83%	81%	79%	88%	82%	86%
10-year	72%	55%	47%	53%	49%	47%	26%	65%	45%	33%
15-year	58%	44%	22%	29%	29%	5%	0%	46%	20%	12%

Conclusions. Technical choices of conduit, graft type, and vessel to be grafted significantly influence CAB graft patency rates. The internal mammary artery is the conduit of choice. When

grafting multiple vessels with one graft, the sequential technique appears to offer better graft survival than do "Y" grafts.

\*By invitation

## **24. CORONARY ARTERY BYPASS GRAFTING WITH THE INFERIOR EPIGASTRIC ARTERY (IEA): MIDTERM CLINICAL AND ANGIOGRAPHIC RESULTS**

Michel Buche, M.D.\*, Jean-Claude Schoevaerdt, M.D.\*, Erwin Schroeder, M.D.\*,  
Olivier Gurne, M.D.\*, Yves Louagie, M.D.\* and Baudouin Marchandise, M.D.\*

*Yvoir, Belgium*

The IEA has been recently used for CABG operations. Histological similarities with the Internal Mammary Artery (IMA) suggest that its patency rate will be comparable to that of free IMA grafts; however, no study has yet validated this assumption.

Material: Between December 1988 and September 1993, 157 patients (141 males, 16 female, mean age: 60.2 years, range 37 to 78 years) underwent a complete myocardial revascularization using 157 IEA, 285 IMA (281 in situ, 4 free grafts). A total of 543 arterial anastomoses (mean 3.4, range 2 to 5 per patient) were constructed, among them 167 with the IEA which was anastomosed to 2 LAD, 5 diagonal, 34 circumflex and 126 RC arteries. The indication for use of the IEA was reoperation in 14 patients, varicose or stripped vein or peripheral arteritis in 42 and a favorable anatomy in 101 selected patients. An early recatheterization was obtained before discharge (mean 11 days postoperatively) in 135 patients, among whom 77 underwent a later angiographic study 6 to 43 months after surgery. A complete follow-up is available for all the patients.

Results: The follow up averages: 26 months (range: 1 to 58 months). Four patients died early and there were 3 perioperative non fatal myocardial infarction (MI). Seven patients required early reoperation for thoracic bleeding (1) or drainage of an abdominal parietal collection (6). There were 4 late deaths (2 sudden deaths, 2 non cardiac causes) and one non fatal MI. Angina recurred in 9 patients of whom 1 required reoperation and 3 underwent successful PTC A of a native coronary artery.

132/135 of the IEA were patent at early control of those 12 showed segmental irregularities or stenotic anastomosis. 44/48 of the IEA restudied within the first postoperative year (mean 8.5 months) were patent however 8 showed a diffuse narrowing. 28/29 of the IEA controlled between 13 and 43 months (mean 25 months) are open and among those 25/29 are widely patent, perfectly matching with the receiving coronary artery. It has to be emphasized that most of the occluded or narrowed IEA were grafted onto coronary arteries with mild stenosis at restudy.

Conclusion: The early attrition rate of the IEA, as for any free arterial graft is probably the result of both the loss of a true pedicle and the need for constructing an additional proximal anastomosis. The improved patency rate beyond one year could suggest a better durability in the future.

**4:45 p.m. EXECUTIVE SESSION (Members Only)**

**East Ballroom**

\*By invitation

**TUESDAY AFTERNOON, APRIL 26, 1994**

**1:45 p.m. SIMULTANEOUS SCIENTIFIC SESSION B - GENERAL THORACIC SURGERY**

**Trianon Ballroom**

**Moderators: John R. Benfield, M.D.**

**J. Kent Trinkle, M.D.**

**25. BILATERAL PNEUMECTOMY (VOLUME REDUCTION) FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

Joel D. Cooper, M.D., Elbert P. Trulock, M.D.\*, G. Alexander Patterson, M.D., Anastasios Triantafillou, M.D.\*, R. Sudhir Sundaesan, M.D.\*, Carolyn M. Dresler, M.D.\* and Charles L. Roper, M.D.

*St. Louis, Missouri*

Surgical options for the treatment of emphysema have included bullectomy for patients with compression of normal underlying lung, and lung transplant for patients with severe disability and limited life expectancy. Based upon observations and experience published 34 years ago by Brantigan, we have undertaken bilateral lung volume reduction surgery in 8 patients with severe emphysema to reduce total thoracic volume and improve chest wall and lung mechanics. All patients had severe functional disability, a distended thorax, and no normal, compressed lung as judged by CT scan. Age range was 39 to 76 years (mean 56). The operation consists of median sternotomy and non-anatomic resection of multiple pieces of lung from either side using a linear stapling device. Portions of lung excised include both bullous and non-bullous areas. All patients have been extubated at the end of the procedure and there has been no early or late mortality. Two patients required re-exploration, one for bleeding and one for persistent air space. Hospital stay was 7 to 48 days (median 15) with persistent air leak the major source of morbidity. Recent use of a buttressed staple line has significantly reduced this complication. There were no sternal wound infections. Followup ranges from 3 to 10 months (mean 6 months).

RESULTS: (Mean values)

<u>FEV<sub>1</sub> liters (% pred)</u>	<u>Pre-Op</u>	<u>Most recent</u>	<u>% Change</u>
FEV <sub>1</sub> -liters(% pred)	0.95 (29%)	1.89 (59%)	†99% (range 64-200% p<001)
RV-liters (% pred)	5.94 (292%)	3.73 (189%)	†37%
TLC-liters (% pred)	8.7 (135%)	7.2 (114%)	†17%
PaO <sub>2</sub> /mmHg (Room air)	65	80	

Supplemental oxygen, required pre-operatively by 4 patients either at rest or with exertion, is not required by any patient. All patients have experienced a dramatic improvement in their quality of life. The early improvement observed in the FEV<sub>1</sub>, has been sustained or further improved in all patients. Our experience to date, though very preliminary, suggests that volume reduction surgery may be a useful therapeutic modality in carefully selected patients, including some for whom this procedure may be a "bridge" to future lung transplantation.



\*By invitation

## **26. SS-LOBECTOMY: A SAFE TECHNIQUE FOR VATS**

Ralph J. Lewis, M.D.

*New Brunswick, New Jersey*

Currently, VATS techniques are being borrowed from the open conventional thoracotomy, however, these same techniques have made VATS lobectomy difficult, burdensome and even dangerous. SS-Lobectomy (Simultaneous Stapling of all hilar structures in their natural anatomical configuration), has been performed successfully in 16 patients. Every attempted SS-Lobectomy is included. There were 14 malignancies, 1 giant benign pulmonary cyst and 1 large necrotizing granuloma. Three RUL, 6 RLL, 4 LUL, 2 LLL and 1 RML were resected uneventfully. Nine adenocarcinoma, 2 large cell carcinomas and 3 squamous cell carcinomas ranging in size from 2.5 to 5 cms were removed. Lung fissures, hilum and mediastinum were explored for lymph nodes in each patient. Median operative time was 110 minutes. Average blood loss was less than 100 ccs. Median hospitalization was 6 days, however, eight patients were discharged between 3 and 5 days. Three patients had air leaks averaging 14 days and one patient had mild subcutaneous emphysema for 5 days. There was no surgical mortality. Median follow-up is 15 months (range 8 to 20 months). SS-Lobectomy is not meant to replace the conventional lobectomy by open thoracotomy. Indications are cardiac or renal problems, contralateral chest wall paralysis, neurogenic deficiencies, adamant refusal of open lobectomy (psychological aberrations, pain from a previous thoracotomy). Contraindications include absent fissures, enlarged matted invasive nodes, fibrotic hilum, central or bulky lesions, calcific bronchi, chest wall invasion or lesions crossing a fissure. Precedent for this technique will be discussed.

Possibly, when used with discretion in certain carefully selected patients, in whom an open lobectomy would be contraindicated, SS-Lobectomy might eventually prove to be another available option. Time and further experience will be necessary to determine its true merits.

\*By invitation

## **27. SUBXIPHOID PERICARDIAL WINDOW FOR PERICARDIAL TAMPONADE: SAFE, COST EFFECTIVE AND DURABLE**

Darroch W.O. Moores, M.D.\*, Keith B. Allen, M.D.\*, David J. Gillman, P.A.\*,  
William H. Warren, M.D. Stanley W. Dziuban, M.D.\*, Riivo Ilves, M.D.\* and L.  
Penfield Faber, M.D.

*Albany, New York and Chicago, Illinois*

Due to recent reports and enthusiasm for VATS pericardectomy we reviewed our experience with subxiphoid pericardial window. From 8/15/88 to 6/7/93 155 patients underwent subxiphoid pericardial window for pericardial effusion associated with pericardial tamponade. There were 85 females (55%) and 70 males ranging in age from 5 weeks to 88 years. The procedure was carried out under general anesthesia in 113 patients (72%), local/sedation in 42 patients. Underlying malignancy was present in 82 patients, 73 patients had benign disease. Follow-up is complete in all patients. The overall 30 day mortality was 20%. The 30 day mortality in patients with malignancy was 32.9% (27/82) versus 5.4% (4/73) for patients with benign disease. None of the post-operative

deaths were attributed to the surgical procedure. Recurrent pericardial effusion requiring further surgical intervention occurred in four patients (2.5%), two with malignancy (2.4%) and two with benign disease (2.7%). Median survival in patients with benign disease was 482 days versus 83 days in patients with malignancy. ( $P < .01$ ) Median survival in patients with malignancy who had proven malignant pericardial effusion was 54 days compared to 95 days for patients with malignancy who did not have tumor in the pericardium. ( $P < .01$ ) Conclusion: 1. Subxiphoid pericardial window is the procedure of choice for patients with pericardial effusion and pericardial tamponade. It can be done under local anesthesia and does not require single lung anesthesia for collapse of the lung. These are important considerations in critically ill patients with pericardial tamponade. 2 Transsthoracic pericardial window by open or video assisted technique offers no benefit over the subxiphoid approach. 3. Following pericardial drainage, survival is significantly shorter in patients with malignant pericardial effusion compared to patients with malignancy who do not have tumor in the pericardium.

### **2:45 p.m. INTERMISSION - VISIT EXHIBITS**

\*By invitation

### **3:15 p.m. SIMULTANEOUS SCIENTIFIC SESSION B - GENERAL THORACIC SURGERY**

**Trionon Ballroom**

**Moderators: John R. Benfield, M.D.**

**J. Kent Trinkle, M.D.**

### **28. CRITICAL ISSUES IN PEDIATRIC LUNG TRANSPLANTATION**

John M. Armitage, M.D., Geoffrey Kurland, M.D.\* , Marian Michaels, M.D.\* , Lynne Cipriani, R.N.\* , F. Jay Fricker, M.D.\* and Hartley P. Griffith, M.D.

*Pittsburgh, Pennsylvania*

Lung transplantation in children is a feasible, safe and effective form of therapy for end stage lung disease. Forty children (age 1-18 years, 27 female and 13 male) have undergone heart-lung(21), double lung(17) and single lung(2) transplant procedures at our center from 1985 through October 1993. The indications for transplantation have been diverse, primary pulmonary hypertension (10), cystic fibrosis (CF) (11), congenital heart disease (CHD) (10), arteriovenous malformation (3), emphysema (1), graft versus host disease (1), rheumatoid lung (1), cardiomyopathy (1), desquamative interstitial pneumonitis (1) and Proteus syndrome (1). The actuarial 1 year survival was 75% (mean follow-up 2 years). One year actuarial survival for disease groups ranged from 60% for CF to 88% for CHD. Despite these gratifying results, we have identified 6 issues critical to the survival of pediatric lung transplantation, to both the individual patients and to the programs themselves. Our experience and management strategies in these areas are reviewed: CYTOMEGALOVIRUS (CMV): 6/8 (75%) CMV mismatched patients (Donor +/- Recipient -) and 7/32 patients who survived greater than 30 days (23%) developed CMV disease. All but CMV Donor -/ Recipient - patients were treated with ganciclovir for 4 weeks posttransplant. We are presently investigating the use of adjuvant CMV specific immunoglobulin. OBLITERATIVE BRONCHIOLITIS (OB): 5/32 (16%) patients who survived greater than 30 days developed OB. OB was manifest within the first posttransplant year as a rapid decline in small airway function. Aggressive augmentation of immunosuppression has been used with little success. POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD): 5/32

(16%) patients who survived greater than 30 days developed PTLD. One patient died (17% mortality) despite retransplantation. Four patients resolved their PTLD with reduction in immunosuppression alone, and 1 required the addition of alpha-interferon. We now obtain donor and recipient EBV serology in all lung transplants. CYSTIC FIBROSIS: CF is the leading indication for lung transplantation in children and carries the highest risk, in the form of infection. We have thus changed our management strategies to avoid triple drug immunosuppression, perioperative blood and bronchial cultures, aggressive antimicrobial therapy, and exclusion of patients with panresistant organisms; this has resulted in elimination of infectious mortalities thus far in the pediatric CF group. AIRWAYS: In 21 heart-lung recipients with tracheal anastomoses we have had no airway complications. The double and single lung transplant recipients accounted for 34 bronchial and 1 tracheal anastomoses. There were 3/34 (9%) bronchial stenoses. Two were treated with silastic stents and 1 with balloon dilatation. FINANCES: The average charge for lung transplant evaluation was \$18, 000 and for transplantation, \$175, 000. The future and success of pediatric lung transplantation will depend upon improved recognition and aggressive prophylaxis and therapy in these 6 critical areas.

\*By invitation

## 29. IMPROVED RESULTS OF LUNG TRANSPLANTATION FOR END STAGE CYSTIC FIBROSIS

Thomas M. Egan, M.D.\*, Frank C. Detterbeck, M.D.\*, Michael R. Mill, M.D.\*,  
Jeanette T. Thompson, B.S.N.\*, Linda J. Paradowski, M.D.\* and Benson R. Wilcox,  
M.D.

*Chapel Hill, North Carolina*

Although cystic fibrosis (CF) patients (pts) are thought to be at high risk for lung transplantation (LTX) because of the infectious nature of their disease and their nutritional status, our experience would suggest otherwise. Since Oct. 1990, 39 CF pts have undergone double LTX (17 males, 22 females; mean age 23, range 8-45; mean weight 75% expected). Immunosuppression consisted of cyclosporine, azathioprine, antilymphocyte globulin, and prednisone, begun two weeks postop. Three pts required retransplant - 2 for primary graft failure and 1 for obliterative bronchiolitis (OB) at 14 months. All pts were colonized with resistant *Pseudomonas* (P) aeruginosa, and 6 harbored P cepacia pre-LTX. Six LTX procedures were performed on ventilated pts. Bilateral sequential implantation was used with bronchial omentopexy. Graft ischemic times were  $303 \pm 9.3$  min for the first implanted lung and  $456 \pm 13.2$  min for the second (mean  $\pm$  SEM). Cardiopulmonary bypass was required for 6 procedures in 5 pts and was associated with increased blood transfusions, compared to LTX performed without it. There have been no operative deaths; three pts died within the first 6 months, two from P cepacia pneumonia and one, unexplained increased intracranial pressure. Of the four pts with partial airway dehiscence, three healed and one was retransplanted. Two pts required temporary dialysis for postoperative renal failure. Hospital stay averaged 30 days (range 14-129 days). One year actuarial survival is 83%. Pre-and postoperative FVC, FEV-1 and actuarial survival of recipients is tabulated (mean  $\pm$  SEM).

% predicted	Pre-op	6 mo.	12 mo.	18 mo.	24 mo.
FVC	$38 \pm 1.7$	$75 \pm 3.6$	$74 \pm 4.4$	$78 \pm 5.3$	$81 \pm 4.8$
FEV-1	$21 \pm 0.8$	$75 \pm 3.8$	$71 \pm 5.3$	$76 \pm 7.3$	$80 \pm 8.5$
Actuarial survival		94%	83%	71%	66%
n surviving	39	26	22	17	10

Survivors have returned to an active lifestyle off oxygen. Infection-related morbidity in CF pts is the same as that for pts with other LTX indications. Of 26 pts surviving beyond 6 months, 11 developed OB, which led to late death in 4 pts. Non-compliance contributed to two of these deaths. Other causes of late death include suicide (1), lymphoma (1), and CMV pneumonia after retransplant for OB (1). LTX can be successfully performed in end stage CF pts with acceptable morbidity and mortality.

\*By invitation

### 30. EXPLORATORY ANALYSIS OF TIME-DEPENDENT RISK FOR INFECTION, REJECTION AND DEATH AFTER PULMONARY TRANSPLANTATION

Ko Bando, M.D.\*†, Irvin L. Paradis, M.D.\*, Robert L. Hardesty, M.D., John M. Armitage, M.D., Kanshi Komatsu, M.D.\*, Hiroaki Konishi, M.D.\*, Robert J. Keenan, M.D.\*, Henry T. Bahnon, M.D. and Bartley P. Griffith, M.D.

*Rochester, Minnesota and Pittsburgh, Pennsylvania*

**Background:** Infection and rejection remain the greatest threat to the survival of pulmonary allograft recipients. Furthermore, there is a complex relationship between infection and rejection in these patients since occurrence of one may predispose to the other. **Methods and Results:** Using a multivariate analysis for repeated events, we analyzed risk factors for treated infection, acute rejection (AR; % grade II) and death among 200 recipients who received 210 pulmonary transplants between January 1988 and March 1993. A total of 76 deaths, 432 AR episodes, and 279 distinct infectious episodes occurred during a follow-up of 6 to 69 months. The pattern of AR after transplant was triphasic, characterized by an early period of higher risk (greatest during the first month), a second lower risk period at 2.3 years (midterm), and a low constant risk. The pattern of infection also appeared triphasic, with a delayed, early phase (peak at 3 months post-op), a period of increased risk at 2.5 years post-op, and a late constant phase. By multivariate analysis, risk factors for AR early after transplantation were donor/recipient cytomegalovirus (CMV) mismatch ( $p=0.0001$ ), longer donor organ ischemia ( $p=0.001$ ) and older donor age ( $p=0.01$ ). Risk factors for AR during the midterm and constant hazard phase included longer donor organ ischemic time ( $p=0.004$ ), symptomatic CMV disease after transplant ( $p=0.01$ ), greater donor/recipient HLA mismatch (HLA-A, B, or DR) ( $p<0.01$ ), older donor age ( $p=0.01$ ), and multiple previous rejection episodes ( $p=0.03$ ). A risk factor for early infection was an episode of significant AR (% Grade II) ( $p=0.001$ ), while risk factors for late infection included frequent episodes of significant AR ( $p=0.001$ ), previous symptomatic CMV disease ( $p=0.001$ ) and frequent episodes of bacterial infection ( $p=0.01$ ). Multiple regression analysis demonstrated that eventual nonsurviving patients had significantly higher rates of AR and infection during both the early and late phases compared with survivors ( $p<0.05$ ). The increased rate of AR among nonsurvivors was evident throughout follow-up, although no deaths were attributable directly to AR after the first 9 months. **Conclusion:** These data suggest that CMV disease, donor ischemic time and donor age affect the incidence of early and late AR. Incidence of infection is increased with repeated episodes of AR. A complex interrelationship between infection and AR determines late survival after pulmonary transplantation.

†1991-1992 Graham Fellow

\*By invitation

**31. SUCCESSFUL OUTCOME OF LUNG TRANSPLANTATION IS NOT COMPROMISED BY THE USE OF MARGINAL DONOR LUNGS**

Sudhir Sundaresan, M.D.\*, Janice Semenkovich, M.D.\*, Elbert P. Trulock, M.D.\*,  
 Laura Ochoa, R.N.\*, Greg Richardson, R.N.\*, Joel D. Cooper, M.D. and G. Alexander  
 Patterson, M.D.  
*St. Louis, Missouri*

Lung transplantation is limited by a shortage of suitable donors. To address this shortage, we have begun utilizing donor lungs which do not meet our previous rigorous donor criteria. Of 100 consecutive lung transplants performed between June 1991 - August 1993, 68 donor lungs were considered ideal as they satisfied all of the following accepted donor criteria (Group I); Age < 55; Smoking < 20 pack years; PaO<sub>2</sub> > 300 mm Hg (using FIO<sub>2</sub> = 1.0 and positive end-expiratory pressure 5 cm H<sub>2</sub>O); and chest radiograph negative for ipsi - or contralateral infiltrate or trauma (contusion or pneumothorax). 32 lungs were considered marginal (Group II) based on criteria shown in the following table:

	Age > 55 years	Smoking > 20 Pack Years	Unsatisfactory Chest Radiograph	PaO <sub>2</sub> < 300mmHg
Group I (n=68)	0	0	0	0
Group II (n=32)	2	6	24	6

53 single lung transplants (SLT) were performed (Group I, 37 vs. Group II, 16) compared to 47 bilateral sequential transplants (BSLT; Group I, 31 vs Group II, 16). In 17 cases in Group II, one or both transplanted lungs contained contusion or infiltrate. Recipient outcome, summarized in the following table, did not differ significantly between the groups:

	<u>Group I (n=68)</u>	<u>Group II (n=32)</u>
A-aDO <sub>2</sub> - immediate	318 ± 138	297 ± 145
A-aDO <sub>2</sub> - 24 hours	159 ± 118	162 ± 129
Days Ventilated	6.9 ± 11.2	8.0 ± 16.1
Death < 30 days	3/68 (4%)	0/32 (0%)
Current Survival	57/68 (84%)	27/32 (84%)

Cardiopulmonary bypass was required to facilitate second graft insertion in 5/31 BSLT in group I (16%) compared to 4/16 BSLT in group II (25%). On the basis of these data, we conclude that successful outcome of lung transplantation can be achieved with the use of marginal donor lungs.

**4:45 p.m. EXECUTIVE SESSION (Members Only)**

**East Ballroom**

\*By invitation

**TUESDAY AFTERNOON, APRIL 26, 1994**

**1:45 p.m. SIMULTANEOUS SCIENTIFIC SESSION C - CONGENITAL HEART DISEASE**

**West Ballroom**

**Moderators: Edward L. Bove, M.D.**

**William G. Williams, M.D.**

**32. DOES THE ROSS OPERATION PROVIDE A DEFINITIVE SOLUTION FOR CHILDREN WITH COMPLEX LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION?**

Jan M. Quaegebeur, M.D., David Solowiejczyk, M.D.\*, Daphne Hsu, M.D.\*, François Bourlon\*, John Hess\* and Welton Gersony, M.D.\*

*New York, New York; Monaco and Rotterdam, The Netherlands*

Since 1988, thirty-three children (age 6 weeks - 15 years) underwent aortic root replacement with a pulmonary autograft (Ross operation) and their survival at five years was 100%. The primary lesion was valvar stenosis (12), hypoplastic aortic annulus (7), long segment LVOTO (9) and aortic incompetence (5). The patients with stenotic lesions had undergone previously 10 balloon dilatations and 39 surgical interventions, amongst them 2 Konno operations. In addition to the Ross operation, the LVOT was enlarged with a pericardial patch in 2 patients, and with a septal incision, using the RV muscle of the autograft to augment the septum in 5 patients. Enucleation of fibromuscular obstruction was performed in 4, repair of aortic arch stenosis in 1, and closure of residual VSD in 1 patient. The Ross operation was always done as a root replacement. Aortic and pulmonary allografts were used for RVOT reconstruction.

Most recent post-operative Echo-Doppler studies of the LVOT estimated gradients of 0-10mm Hg in 20 patients, 10-20mm Hg in 2 and 20-30mm Hg in 1 patient. Neo-aortic incompetence was absent or trivial in 30 patients, mild in 2 and moderate in 1. The degree of neo-aortic incompetence in the latter 3 patients was present early postoperatively and has not progressed with time. There were no gradients across the RVOT in 22 patients, 10-20mm Hg in 9, 20-30mm Hg in 1. In 1 patient the gradient was 70mm Hg and he was reoperated for allograft replacement. No other reoperations were required. In 20 patients, serial echo measurements have been obtained. Increase in size of the neo-aortic root was demonstrated in all. In 15 patients this enlargement was appropriate for the patients increase in BSA, supporting growth of the autograft. However, in 5 patients the autograft had become larger than expected for their BSA, suggesting an element of dilatation.

In conclusion, the Ross operation provides excellent relief of complex LVOTO in children of all ages. With appropriate growth of the autograft, in the absence of future structural failure, it appears likely that the Ross procedure is a definitive operation. Autografts which are larger than anticipated will require careful follow-up, and the fate of the allograft in the RVOT remains uncertain.

\*By invitation

**33. LATE RESULTS OF SYSTEMIC ATRIOVENTRICULAR VALVE REPLACEMENT IN CORRECTED TRANSPOSITION**

Jacques A.M. van Son, M.D.\*, Gordon K. Danielson, M.D., James C. Huhta, M.D.\*, James B. Seward, M.D.\*, Hartzell V. Schaff, M.D., Francisco J. Puga, M.D. and Duane M. Ilstrup, M.S.\*

*Philadelphia, Pennsylvania and Rochester, Minnesota*

From 1964 through 1992, 40 patients (aged 5 months to 70 years, median 13.6 years) with corrected transposition of the great arteries and systemic atrioventricular (AV) valve insufficiency underwent replacement (n = 39) or repair (n = 1) of the systemic AV valve. Thirty-nine patients had situs solitus and one had situs inversus. Associated anomalies included

Ebstein's malformation of the systemic AV valve (n = 22), ventricular septal defect (n = 10), and pulmonary stenosis (n = 14). Preoperatively, 16 patients (40.0%) had complete heart block and 27 patients (67.5%) were in New York Heart Association (NYHA) functional classes III and IV. The hospital mortality was 10.0% (n = 4), and 8 patients died subsequently. Overall survival was 74.5% at 5 years and 59.3% at 10 years. The principal cause of death was systemic ventricular failure in 12 patients. Survivorship correlated with systemic ventricular ejection fraction of 44% or more (p<0.001) and later interval of operation (9 deaths in 15 patients (60.0%) before 1981 versus 3 deaths in 25 patients (12.0%) subsequently) (p=0.06). There was no surgically-induced complete heart block. Two patients underwent late reoperations related to the systemic AV valve prosthesis. Follow-up extended to 26.0 years (median = 4.3 years). At last follow-up, 18 of the 28 survivors were in NYHA functional class I, 9 were in class II, and 1 was in class III. We conclude that the results of systemic AV valve replacement in corrected transposition have improved significantly during the last decade. In order to preserve systemic ventricular function, operation should be considered at the earliest sign of progressive ventricular dysfunction as assessed by serial clinical evaluation and echocardiography.

\*By invitation

#### **34. SURGERY FOR CONGENITALLY MALFORMED MITRAL VALVE IN INFANCY**

Miguel Sousa Uva, M.D.\*, François Lacour-Gayet, M.D.\*, Jaqueline Bruniaux, M.D.\*, Alain Serraf, M.D.\*†, Jean Paul Binet, M.D. and Claude Planche, M.D.  
*Paris, France*

Congenital mitral valve disease presenting in infancy is rare and surgery is seldom indicated in view of its poor results. However, severe refractory cardiac failure due to mitral incompetence or stenosis, may occasionally require early surgical treatment. The aim of this study was to assess indications and outcome of mitral valve repair in the first year of life.

All patients (pts) less than one year old operated for congenital mitral valve incompetence (MI) (n=10) or congenital mitral stenosis (MS) (n=5) between 1980 and 1993 were retrospectively analysed. Pts with discordant A-V connection, A-V canal defect, cor triatriatum, supra-avalvular mitral ring or class III/IV hypoplastic left heart syndrome were excluded. Mean age at operation was 6.5 months. Indication was severe heart failure resistant to medical treatment and grade 4/4 MI, or mean pulmonary artery pressure >45 mmHg. Associated DORV with subaortic stenosis (n=2), VSD (n=3), aortic stenosis (n=2) and coarctation (n=2) were previously or concomitantly treated. Valve repair was performed in all 10 MI and 3 MS; valve replacement was required in two pts with parachute mitral valve. Repair included, among other procedures, Wooler or de Vega type annuloplasty and mobilisation of the subvalvular apparatus.

There were no early deaths. Three MI pts required early reoperation with valve replacement in two and re-repair in one. One patient with MS required valve replacement at 6 months and died. No other late deaths occurred. Follow up has been one month to 10 years (mean=50 months). Eleven pts were in NYHA class I and 3 were in class II. Doppler echocardiography at latest follow up after valvuloplasty was available in 8 pts and showed minimal MI in 3 pts, mild MI in 3 and moderate MI in 2; two pts had a maximum trans mitral gradient of 10 mmHg. These results show that : 1) valve repair for congenital MI in infancy can be performed with satisfactory functional results and low operative risk although some patients will require reoperation. 2) MS remains a surgical challenge, reparative procedures being palliative and valve replacement most often unavoidable.

**2:45 p.m. INTERMISSION - VISIT EXHIBITS**

†1993-1994 Graham Fellow

\*By invitation

### **3:15 p.m. SIMULTANEOUS SCIENTIFIC SESSION C -CONGENITAL HEART DISEASE**

**West Ballroom**

**Moderators: Edward L. Bove, M.D.**

**William G. Williams, M.D.**

#### **35. LONG-TERM FOLLOWUP OF EXTENDED AORTOPLASTY FOR SUPRA VALVULAR AORTIC STENOSIS**

Ralph E. Delius, M.D.\*, John B. Steinberg, M.D.\*, Thomas J. L'Ecuyer, M.D.\*, Donald B. Doty, M.D. and Douglas M. Behrendt, M.D.

##### ***Iowa City, Iowa and Salt Lake City, Utah***

Extended aortoplasty is an operation that was designed to provide a symmetric reconstruction of the aortic root in patients with discrete supravalvular aortic stenosis. The aim of this report is to provide long term followup of the original cohort of patients undergoing this operation. Fifteen patients underwent extended aortoplasty between 1977 and 1983. Followup was obtained in fourteen patients. One patient was lost to followup 3 years after operation; he was included in this report. An echocardiogram, chest radiograph, and electrocardiogram were obtained for each surviving patient. The median length of followup was 141 months (range 36-238). The median preoperative gradient was 90mm Hg (range 55-150). The median immediate postoperative gradient was 20mm Hg (range 0-50,  $p<0.05$  compared to preoperative gradient) and the median long term gradient was 32mm Hg (range 6-96,  $p<0.05$  compared to preoperative gradient,  $p=NS$  compared to immediate postoperative gradient). Two patients died during the period of followup, one from left ventricular failure following an aortic valve replacement and one from chronic left ventricular failure. The Kaplan-Meier estimate of survival at 169 months for all patients was 77.4% (70% CL 62-93%). The estimated freedom from reoperation for all patients was 60% at 141 months (70% CL 56-82%). Univariate analysis revealed that the presence of a bicuspid valve is a significant risk factor for reoperation ( $p=0.038$ ), but not for death ( $p=0.51$ ). The Kaplan-Meier estimate of freedom from reoperation for patients with a bicuspid aortic valve was 42.9% at 141 months (70% CL 21-65%). Extended aortoplasty provides effective long term relief of the pressure gradient across the supravalvular ridge. However, a significant number of patients require subsequent operations, particularly those with a bicuspid aortic valve.

\*By invitation

#### **36. CRITICAL AORTIC STENOSIS: A COMPARISON OF BALLOON VALVULOPLASTY AND TRANSVENTRICULAR DILATATION**

Ralph S. Mosca, M.D.\*, Mark D. Iannettoni, M.D.\*, Steven M. Schwartz, M.D.\*, Robert H. Beekman, III, M.D.\*, Achi Ludomirsky, M.D.\* and Edward L. Bove, M.D.

##### ***Ann Arbor, Michigan***

The optimal treatment of critical aortic stenosis in the neonate and young infant remains controversial. We retrospectively reviewed our experience with transventricular dilatation (TVD)



utilizing normothermic cardiopulmonary bypass and balloon valvuloplasty (BV) with respect to early and late survival, relief of aortic stenosis, degree of aortic insufficiency, left ventricular function, and freedom from reintervention. Between July 1987 and July 1993, 24 neonates and infants underwent either TVD (n = 17) or BV (n = 7) for critical aortic stenosis. The patients in the TVD group were older (mean age, 18 days; range, 1-59 days) when compared with the BV group (mean age, 10 days; range, 1-31 days), p=.05. There were no significant differences in left ventricular function, degree of left ventricular outflow tract obstruction, or aortic annulus size between the groups. Associated anomalies were more common in the TVD group (53%) compared to the BV group (13%), p=.05. Following treatment, the mean reduction in aortic gradient and the degree of aortic insufficiency were equivalent in both groups as assessed by Doppler/echocardiography. Ejection fraction improved significantly in both groups (TVD, 39 ± 5.0% vs 46 ± 5%; BV, 51 ± 2% vs 62 ± 3%) but there was no statistical difference between groups. The LV mass to volume ration (gm/cc<sup>3</sup>) also increased significantly in both groups but with no significant difference between groups (TVD, 1.2 ± 0.5 vs 1.6 ± 0.6; BV, 1.1 ± 0.6 vs 1.5 ± 0.4). Early mortality in the TVD group was 9.5% and in the BV group 14% (p=ns). There were no late deaths in either group. Three patients from the TVD group and 2 patients from the BV group required reintervention for further relief of aortic stenosis. We conclude that both TVD and BV provide adequate and equivalent relief of critical aortic stenosis. Treatment strategies should therefore depend upon other factors including the presence of associated cardiovascular anomalies, vascular access, preoperative condition and the local expertise of the institution.

\*By invitation

### **37. COARCTATION OF THE AORTA PRESENTING FOR TREATMENT IN NEONATES**

John W. Kirklin, M.D., Jan M. Quaegebeur, M.D., Richard A. Jonas, M.D., Alan D. Weinberg, M.S.\* and Eugene H. Blackstone, M.D.

*Birmingham, Alabama; New York, New York and Boston, Massachusetts*

Among the 322 neonates with coarctation, with or without a ventricular septal defect (VSD) and in a multi-institutional study, survival for at least 24 months after an initial procedure was 84%. Other coexisting obstructive lesions in the left heart-aorta (LHA) complex decreased survival; these included mitral valve anomalies in 5% of patients, left ventricular hypoplasia in 5%, narrowing of the left ventricular outflow tract in 9%, and narrowing of the proximal arch in 1%. The most commonly used technique of repair of the coarctation was resection and end-to-end anastomosis, but no technique was a risk factor for death by multivariable analysis. Extension of the area of resection so that the end-to-end anastomosis was proximal to the left subclavian artery but distal to the left common carotid artery, did not increase risk. Neonates without other coexisting obstructive lesions in the LHA complex, and without or with small VSD, have a 97% survival for at least 24 months after end-to-end anastomosis, or subclavian flap repair, or patch graft repair; among those with coexisting moderate-sized or large VSDs, repair of the VSD and pulmonary trunk (PT) banding was associated with the highest 2-year survival, 97% in those with single VSD (Figure).

The risk-adjusted outcomes in two institutions were believably less; good than in all others. Therapeutic inferences are that critically ill neonates with coarctation without or with small VSD do well with surgical repair of the coarctation as initial treatment. Those with moderate-sized or large VSD do best with initial repair of the coarctation and PT banding (often with subsequent repair of the VSD at the same hospitalization). Concomitant procedures against a coexisting obstructive lesion in the LHA complex are rarely indicated.

\*By invitation

### **38. VIDEO-ASSISTED THORACOSCOPIC SURGERY FOR CONGENITAL HEART DISEASE**

Redmond P. Burke, M.D.\*, Mary VanderVelde, M.D.\*, Dolly Hansen, M.D.\* and Gil Wernovsky, M.D.\*

*Boston, Massachusetts*

Video-assisted thoracoscopic surgery (VATS) provides excellent visualization of anatomic structures, causes minimal surgical trauma, and has significantly expanded surgical options in adult thoracic surgery. VATS applications in children with congenital heart disease have been limited to patent ductus arteriosus interruption. After designing endoscopic instruments for pediatric thoracoscopic cardiovascular use, and extensive animal experimentation, video-assisted techniques were developed for 7 different surgical procedures in children, including: Interruption of patent ductus arteriosus (N=14), division of vascular ring (N=4), drainage of posterior pericardial effusion (N=3), interruption of arterial and venous collaterals (N=2), thoracic duct ligation (N=1), epicardial pacemaker lead insertion (N=1), and diagnostic thoracoscopy (N=1). Ages of these 26 patients ranged from 2 hours to 12 years, and weights from 575 grams to 46 kilograms. There was no operative mortality. Five patients (19%) required conversion to thoracotomy to complete procedures including: vascular ring division (N=2), pericardiectomy (N=1, PDA interruption (N=1) and epicardial pacemaker lead placement (N=1). One recurrent laryngeal nerve injury (4%) occurred during PDA interruption. Patients undergoing elective VATS for vascular ring division and PDA ligation were extubated in the operating room and discharged from the hospital within 48 hours. With a comprehensive program, VATS can be successfully applied to a widening range of cardiovascular problems afflicting neonates and infants.

**4:45 p.m. EXECUTIVE SESSION (Members Only)**

#### **East Ballroom**

\*By invitation

## **WEDNESDAY MORNING, APRIL 27, 1994**

**7:00 a.m. FORUM SESSION II - Grand Ballroom**

**Moderators: Frederick L. Grover, M.D.**

**Robert A. Guyton, M.D.**

### **F10. CAN DONOR HEARTS BE GENETICALLY ALTERED PRIOR TO TRANSPLANTATION?**

Abbas Ardehali, M.D.\*, Hillel Laks, M.D., Alistair I. Fyfe, M.D.\*, Davis C.

Drinkwater, M.D.\*, Jian-Hua Qiao, M.D.\* and Aldons J. Lusic, Ph.D.\*

*Los Angeles, California*

Access to the donor heart at the time of harvest provides a unique opportunity for genetic manipulation of this organ prior to transplantation. We sought to determine a) if donor mouse hearts

express a foreign gene administered at harvest, and b) if so, what is the most effective route of gene delivery. At harvest, 30 ug of pCMV-Luciferase DNA plasmid in cationic liposomes was injected I) directly into myocardial apex, or II) into the right atrium, or III) into the coronary arteries. The donor hearts (n=4 in each group) were then transplanted into the abdomen of the recipient mice of the same strain. The transplanted hearts were removed in 96 hours and luciferase expression was assayed by immunohistochemistry. In group I, luciferase activity was localized to the apex. In group II, where plasmid was delivered into the right atrium, luciferase expression was detected solely in the right ventricle endocardium. In group III, where plasmid was injected into the coronary arteries, the transplanted hearts demonstrated luciferase expression in a) perivascular areas surrounding coronary arteries and veins, b) coronary capillaries, and c) the endocardium of both ventricles. Conclusions: This study suggests that a) mouse hearts can be genetically modified at the time of harvest, and b) intracoronary infusion of plasmid yields the most effective method of delivery. Administration of plasmid in the coronary arteries localizes the expression to the endocardium and the coronary vasculature, both sites of immunologic interactions after heart transplantation. Intracoronary infusion of plasmids at the time of harvest may allow genetic modification of the donor hearts in the near future.

\*By invitation

#### **F11. LUNG TRANSPLANTATION USING CARDIO-PULMONARY BYPASS EXAGGERATES PULMONARY VASOMOTOR DYSFUNCTION IN THE TRANSPLANTED LUNG**

David A. Fullerton, M.D.\*, Robert C. McIntyre, M.D.\*, Max B. Mitchell, M.D.\*,  
David N. Campbell, M.D.\* and Frederick L. Grover, M.D.

*Denver, Colorado*

**BACKGROUND:** Pulmonary vascular resistance (PVR) is significantly increased in the transplanted lung. If cardiopulmonary bypass (CPB) is required, the transplanted lung is reperfused with activated blood elements which might exacerbate the reperfusion injury. Therefore, we postulated that pulmonary vasomotor dysfunction is exaggerated when cardiopulmonary bypass is used for lung transplantation. The purpose of this study was to examine the influence of cardiopulmonary bypass on the following mechanisms of pulmonary vasomotor control in a dog model of autologous lung transplantation: (1) Endothelial-dependent cGMP-mediated relaxation (response to Acetylcholine, ACh) (2) Endothelial-independent cGMP-mediated relaxation (response to Nitroprusside, NP) and (3)  $\beta^2$ -adrenergic cAMP-mediated relaxation (response to Isoproterenol, ISO).

**METHODS:** Autologous lung transplants were performed in dogs using (n=4) and without (n=5) CPB. After infusing PGE<sub>1</sub> (10u/kg), modified Euro-Collins solution (4°C, 30cc/kg) was infused into the right pulmonary artery. The right lung was removed, stored in saline (4°C) for 3 hours, then reimplanted and reperfused for one hour. 2 third-order pulmonary arteries were dissected from each lung at each of two times: immediately post harvest (controls) and after one hour of reperfusion. The vasorelaxing effects of ACh  $10^{-6}$ M, NP  $10^{-6}$ M and ISO  $10^{-6}$ M were studied in isolated pulmonary arterial rings, suspended on fine wire tensiometers in individual organ chambers. Vasomotor function was compared in 3 groups: (1) Control (2) Lung Transplant Without CPB and (3) Lung Transplant Using CPB. Statistical analysis was by ANOVA (Sheffe's F-test).

**RESULTS:** As shown below, lung transplantation using CPB produced significantly greater endothelial-dependent as well as -independent pulmonary vasomotor dysfunction than without CPB. Values are Mean  $\pm$  SD.

**CONCLUSION:** Lung transplantation using CPB greatly exaggerates pulmonary vasomotor dysfunction. This may result in significantly higher PVR in the transplanted lung when cardiopulmonary bypass is used.

\*By invitation

## **F12. SUPPLEMENTAL L-ARGININE DURING CARDIOPLEGIC ARREST AVOIDS REGIONAL POSTISCHEMIC INJURY VIA THE L-ARGININE-NITRIC OXIDE PATHWAY**

Hiroki Sato, M.D.\*, Zhi-Qing Zhao, M.D., Ph.D.\*, Jakob Vinten-Johansen, Ph.D.\*, D. Scott McGee, B.S.\* and John W. Hammon Jr., M.D.

*Winston-Salem, North Carolina*

Ischemia and reperfusion impair contractile function and the generation of cytoprotective nitric oxide (NO) by the vascular endothelium. This study tested the hypotheses that blood cardioplegia (BCP) supplemented with the NO precursor L-arginine (L-Arg) would 1) preserve endothelial function, 2) reduce infarct size, and 3) reverse postcardioplegia regional dysfunction by the L-Arg-NO pathway. In 16 anesthetized dogs, the left anterior descending coronary artery (LAD) was ligated for 90 minutes, after which bypass was established for surgical "revascularization." In 9 dogs, unsupplemented multidose hypothermic BCP was administered for a total of 60 minutes of cardioplegic arrest. In 7 dogs, L-Arg was given intravenously (4 mg/kg/min) and in BCP (10 mM) during arrest. Infarct size (TTC) as percent of the area at risk, was less in L-Arg compared to BCP (28  $\pm$  4% versus 41  $\pm$  4%, p=0.04). Postischemic regional segmental work (sonomicrometry) was significantly better in L-Arg (91  $\pm$  15 mmHg-mm) versus BCP (28  $\pm$  3 mmHg-mm, p<0.001). Segmental diastolic stiffness was preserved in L-Arg (0.46  $\pm$  0.06) compared to BCP (1.12  $\pm$  0.11, p=0.0001). In postischemic LAD vascular rings taken from the above experiments, depressed maximum relaxation responses to the receptor-dependent stimulator of NO in BCP group (70  $\pm$  5%) was reversed by L-Arg (92  $\pm$  3%, p=0.002). Smooth muscle function was unaffected in either group. The beneficial effects of L-Arg *in vivo* and *in vitro* were reversed by the NO-synthase inhibitor L-NA ( $10^{-3}$  M). We conclude that L-Arg supplementation during cardioplegia reduces infarct size, preserves acute postischemic systolic and diastolic regional function, and prevents endothelial dysfunction via the L-arginine-NO pathway.

\*By invitation

## **F13. EFFECTS OF L-ARGININE AND L-NAME ON RECOVERY OF NEONATAL LAMB HEARTS AFTER COLD CARDIOPLEGIC ISCHEMIA: EVIDENCE FOR AN IMPORTANT ROLE OF ENDOTHELIAL PRODUCTION OF NITRIC OXIDE**

Takeshi Hiramatsu, M.D.\*, Joseph M. Forbess, M.D.\*, Takuya Miura, M.D.\* and John E. Mayer, Jr., M.D.

*Boston, Massachusetts*

Myocardial ischemia and reperfusion result in both ventricular and endothelial dysfunction. We have found that the endothelial (Endo) defect is a reduced response to acetylcholine (ACh), likely due to reduced nitric oxide (NO) release, but others report that NO is deleterious after ischemia. To investigate the role of NO in recovery after hypothermic ischemia, we examined the effects of infusions of 3mM L-arginine (L-ARG), a NO precursor, 1mM L-nitro-arginine methyl ester (L-NAME), a NO synthase inhibitor, 1mM L-NAME plus 3mM L-ARG and 3mM D-arginine (D-ARG), a stereoisomer of L-ARG vs controls (C) in isolated blood-perfused neonatal lamb hearts subjected to 2 hrs of cold cardioplegic ischemia. L-NAME was given before reperfusion, and L-ARG and D-ARG were infused during the first 20 min of reperfusion. At 30 min of reperfusion, maximal (Max) and volume-normalized (V10) LV developed pressure (DP), +dP/dt, -dP/dt, coronary blood flow (CBF), myocardial oxygen consumption (MVO2) were measured. Endo function was assessed by the coronary vascular resistance (CVR) response to 10-7M ACh and 3x10<sup>-5</sup>M nitroglycerin (NTG). Results are given as % recovery of preischemic values. (\*=p<.05 vs C by Student-Newman-Keuls test)

Group	n	Max			V10		CBF	MVO2	CVR response	
		DP	+dP/dt	-dP/dt	DP	dP/dt			ACh	NTG
C	8	75.5	68.3	60.7	75.1	66.8	133.0	76.1	39.2	42.4
L-ARG	8	94.5*	88.8*	74.1*	90.3*	87.5*	203.2*	96.8	61.0*	36.4
ARG+NAME	8	79.6	69.4	59.6	80.4	71.1	120.7	74.4	29.0	42.1
L-NAME	8	66.4*	54.9*	46.4*	66.1*	55.5*	86.0*	63.0	14.1*	50.7
D-ARG	8	79.4	70.8	62.6	80.8	73.1	140.0	80.7	40.1	38.2

Recovery of all variables in L-ARG was significantly better (p<.05) compared to L-NAME except NTG.

L-ARG, but not D-ARG improved recovery of ventricular function, MVO2, CBF and Endo-mediated response to ACh. L-NAME reduced recovery of ventricular function, CBF and ACh response, and these effects of L-NAME were reversed to equal control values by adding L-ARG to L-NAME treated hearts. These results confirm an important salutary role for Endo production of NO in recovery after hypothermic ischemia in neonatal lamb hearts.

\*By invitation

**F14. PATTERNS OF CHANGES IN NEUTROPHIL ADHESION MOLECULES DURING NORMOTHERMIC CARDIOPULMONARY BYPASS - A CLINICAL STUDY**

Philippe Menasche, M.D., Ph.D.\*, Françoise Le Deist, M.D.\*, François Tronc, M.D.\*, Jacques Larivière, M.D.\*, Armand Piwnicka, M.D. and Gerard Bloch, M.D.\* *Paris, France*

*Background:* Adhesion of activated neutrophils to endothelial cells and their subsequent migration represent key features of the inflammatory response to cardiopulmonary bypass (CPB) involved in postbypass organ dysfunction. However, the molecular mechanisms of this adhesion during *clinical* CPB are still poorly characterized.

*Objective:* To assess the patterns of changes of the two sets of neutrophil adhesion molecules involved in endothelial binding and migration during CPB. One set of these molecules comprises the three activation-triggered  $\beta_2$  integrins referred to as the CD 18 complex (GD11a/CD 18,

GD11b/CD18, GD11c/CD18) and the second set is made up by L-selectin, the peripheral lymph node homing receptor that is normally expressed on unactivated leukocytes.

*Methods:* We studied 8 adult patients who underwent coronary (N=6) or valvular (N=2) operations with the use of normothermic (33°-37°C) CPB and warm blood cardioplegia. A membrane oxygenator was used in all cases. The mean duration of CPB was 91 min (range : 70-132). Arterial blood samples were taken after anesthetic induction, at 5, 10 and 15 min on CPB and 30 min after the end of CPB. Adhesion molecules were detected by direct immunofluorescence evaluated by flow cytometry using a FACScan in log scale. Data (mean  $\pm$  SD) are expressed as mean linear fluorescence.

*Results:* They can be summarized as follows: (1) There was no significant change in GD11a expression throughout the study period; (2) This contrasted with a drastic rise in CD11b expression which started early on bypass (at 10 and 15 min :  $134 \pm 72$  and  $167 \pm 61$  vs  $66 \pm 37$  at baseline,  $p < 0.05$  and  $p < 0.01$  by t tests, respectively) and persisted 30 min after bypass ( $154 \pm 128$ ); (3) Changes in CD11c were less consistent but grossly featured a trend toward an early increase on bypass (at 15 min :  $53 \pm 18$  vs  $36 \pm 13$  before CPB: followed by a return to baseline levels 30 min after CPB ( $42 \pm 22$ )); (4) L-selectin expression decreased during bypass but to a lesser extent than that of GD11b increased (at 10 and 15 min :  $828 \pm 109$  and  $809 \pm 119$ , respectively, vs  $994 \pm 185$  at baseline,  $p = \text{NS}$ ); (5) Finally, postbypass fluorescence histograms disclosed two populations of cells : one expressed CD11b and CD11c above preCPB levels whereas the second had a low expression of the respective epitopes and, therefore, probably corresponds to cells newly released from the bone marrow.

*Conclusion:* These data provide direct molecular evidence that, in human beings, neutrophil activation during CPB causes upregulation of CD11b/CD18 to a greater extent than it causes downregulation of L-selectin, thereby resulting in an enhanced adhesiveness of neutrophils with the potential for neutrophil adhesion-triggered cytotoxic events. From a clinical standpoint, CD11b/CD18 and L-selectin could thus represent elective targets for therapeutic interventions designed to reduce the inflammatory component of post-bypass morbidity.

\*By invitation

## **F15. IMPACT OF INITIAL FLUSH POTASSIUM CONCENTRATION ON THE ADEQUACY OF LUNG PRESERVATION**

Shigeyuki Sasaki, M.D, Ph.D.\*, James D. McCully, Ph.D.\*, Francesca Alessandrini, B.S.\* and Joseph LoCicero, III, M.D.

*Boston, Massachusetts*

Potassium ( $K^+$ ) is a classic pulmonary artery vasoconstrictor, yet most preservation solutions have high  $K^+$  concentrations. We wished to determine the  $K^+$  threshold below which adequate lung preservation could be maintained. We evaluated flush solutions containing physiologic to high dose potassium concentrations. Excised Sprague-Dawley rat lungs ( $n=32$ ) were flushed first with one of following solution: (1) University of Wisconsin solution (UWS;  $K^+=140\text{mM}$ ) (2) Low-potassium UWS (mUWS;  $K^+=20\text{mM}$ ) (3) Dulbecco's Phosphate-Buffered Saline (DPBS;  $K^+=3.9\text{mM}$ ) (4) modified PBS (mPBS;  $K^+=20\text{mM}$ ) (5) Euro-Collins solution (ECS;  $K^+=115\text{mM}$ ), then stored in 4°C UWS for 24 hrs. All lungs were reperfused in the isolated blood perfused working lung system for 2hrs or until lung failure, determined by either blood gas ( $\text{SaO}_2 < 90\%$ ) or appearance of bronchial fluid. Aerodynamic values were measured on airway volume-pressure loop.

Results: (Values at 30min (upper) and 90min (lower) perfusion; mean  $\pm$  SEM)

	UWS (n=6)	mUWS (n=6)	DPBS (n=7)	mPBS (n=7)	ECS (n=6)
pO <sub>2</sub>	56.1 $\pm$ 4.21	72.7 $\pm$ 9.09 <sup>†</sup> 77.6 $\pm$ 9.90	87.7 $\pm$ 6.93 <sup>*†</sup> 88.4 $\pm$ 1.54	108 $\pm$ 9.61 <sup>**‡</sup> 71.0 $\pm$ 11.7	53.5 $\pm$ 6.01
SF	40.6 $\pm$ 8.30	16.4 $\pm$ 4.86 <sup>*†</sup> 13.0 $\pm$ 3.77	12.8 $\pm$ 2.39 <sup>*†</sup> 12.7 $\pm$ 2.58	8.01 $\pm$ 2.17 <sup>**‡</sup> 16.4 $\pm$ 3.07	36.8 $\pm$ 8.69
RA	5.76 $\pm$ 0.93	2.82 $\pm$ 0.16 <sup>*‡</sup> 3.24 $\pm$ 0.50	3.06 $\pm$ 0.17 <sup>*‡</sup> 3.16 $\pm$ 0.19	2.78 $\pm$ 0.23 <sup>**†</sup> 2.85 $\pm$ 0.18	4.95 $\pm$ 0.52
DC	0.13 $\pm$ 0.02	0.23 $\pm$ 0.01 <sup>†</sup> 0.23 $\pm$ 0.03	0.25 $\pm$ 0.02 <sup>*‡</sup> 0.24 $\pm$ 0.02	0.24 $\pm$ 0.02 <sup>‡</sup> 0.24 $\pm$ 0.01	0.17 $\pm$ 0.02
Wel	37.7 $\pm$ 6.84	19.8 $\pm$ 1.49 <sup>‡</sup> 21.4 $\pm$ 3.56	18.7 $\pm$ 1.24 <sup>‡</sup> 18.9 $\pm$ 1.12	19.2 $\pm$ 1.33 <sup>‡</sup> 19.5 $\pm$ 1.18	27.2 $\pm$ 2.55

(pO<sub>2</sub> (mmHg), SF:shunt fraction (%), RA:lung airway resistance (cmH<sub>2</sub>O/ml/sec),

DC:lung compliance (ml/cmH<sub>2</sub>O), Wel:elastic lung work (g-cm);

ANOVA with post hoc pairwise comparisons (Tukey). \*p<0.05, \*\*p<0.01 vs ECS, †p<0.05, ‡p<0.01 vs UWS)

All lungs flushed with ECS or UWS demonstrated failure within 1 hr of reperfusion. These results indicate the superiority of low-potassium flushing solution, either in crystalloid or colloid flushing. We conclude that lung storage with UWS should be preceded by low potassium (K<sup>+</sup><20mM) flushing which can contain colloid.

\*By invitation

#### F16. SERUM CYTOKINES FOLLOWING PEDIATRIC CARDIAC SURGERY: THE ROLE OF INTERLEUKIN-8 IN THE POSTOPERATIVE INFLAMMATORY RESPONSE

Frank W. Mocek, M.D.\* , Laman A. Gray, Jr., M.D., Michael J. Edwards, M.D.\* and

Erie H. Austin, III, M.D.\*

*Louisville, Kentucky*

Sequelae related to cardiopulmonary bypass (CPB) following pediatric cardiac surgery is an important source of early postoperative morbidity. The purpose of this study was to determine the change in serum cytokine levels over time and to correlate these changes with known parameters of the inflammatory response in the pulmonary system.

METHODS: Serum cytokine levels including Tumor Necrosis Factor (TNF), Interleukin (IL)-1, IL-6, and IL-8 were measured by ELISA prior to, and at intervals following induction of CPB in 18 consecutive patients undergoing correction of congenital anomalies.

RESULTS	Baseline	5 min	1 hr	24hrs	48hrs
TNF	1.2 $\pm$ 0.70	1.5 $\pm$ 1.2	3.0 $\pm$ 2.5	2.7 $\pm$ 2.5	3.1 $\pm$ 2.5

IL-1	0.6 ± 0.3	0.4 ± 0.2	0.4 ± 0.3	0.4 ± 0.2	0.4 ± 0.1
IL-6	2.6 ± 0.8	4.4 ± 2.1	65.2 ± 19.0*	50.0 ± 11.7*	25.2 ± 5.3
IL-8	30.0 ± 5.6	81.6 ± 23.8	227.0 ± 46.4*	75.7 ± 31.0	112.3 ± 62.7

(All data expressed mean ± S.E.M., pg/ml; groups compared by ANOVA, correlations by linear regression analysis, (\*) p<.05 considered significant.)

IL-6 reached peak serum levels at 1 hr (p<.05) and remained significantly elevated at 24 hrs (p<.05) but then decreased significantly from peak levels by 48 hrs (p<.05). Serum IL-8 was significantly increased at 1 hr (p<.05) but declined significantly by 24 hrs (p<.05) following CPB. Furthermore serum IL-8 levels were directly correlated with length of CPB time (p<.001), pulmonary neutrophil sequestration at 1 hr (p<.001) and the presence of pulmonary edema at 24 hrs (p<.001) and 48 hrs (p<.001). Serum IL-8 was also closely correlated with intraoperative fluid requirements (p<.001) and fluid requirements at 24 (p<.001) and 48 hrs (p<.001).

**CONCLUSION:** These data demonstrate that production of IL-6 and IL-8, but not TNF or IL-1, is initiated shortly after the induction of CPB. Serum IL-6 levels remain elevated for at least 24 hrs suggesting production of this cytokine continues throughout this period. In contrast, serum IL-8 levels decreased significantly by 24 hrs following the peak at 1 hr. The strong correlation between IL-8 and pulmonary neutrophil sequestration, pulmonary edema, and increased fluid requirements suggest IL-8 may be an integral mediator in the inflammatory response resulting in pulmonary dysfunction following CPB. Options for protection should be considered.

\*By invitation

## **F17. ENDOTHELIAL-LINED SKELETAL MUSCLE VENTRICLES IN CIRCULATION**

Gregory A. Thomas, M.D.\*, Peter I. Lelkes, Ph.D.\*, Susumu Isoda, M.D., Ph.D.\*,

Dawn Chick, B.S.\*, Huiping Lu, M.D.\*, Robert L. Hammond, B.S.\*, Hidehiro

Nakajima, M.D., Ph.D.\*, Hisako Nakajima, M.D.\*, Henry L. Walters, III, M.D.\* and

Larry W. Stephenson, M.D.

*Detroit, Michigan and Milwaukee, Wisconsin*

Skeletal muscle ventricles (SMVs) are muscular pumping chambers connected to the circulation for cardiac assist. In our lab, SMVs have functioned routinely in the circulation for over 6 months; in 1 dog an SMV pumped blood continuously for 836 days. However, during chronic, in-circulation studies, thrombus has formed inside many of the SMVs with subsequent thromboembolism. In order to decrease the incidence of thrombosis, we have been lining SMVs with autogenous endothelial cells; in a group of 7 dogs seeded with autogenous endothelial cells, an 80-100% complete monolayer of endothelium was obtained. For this study, SMVs were constructed from the latissimus dorsi in 6 dogs by wrapping the muscle around a polypropylene mandrel. Jugular vein endothelial cells were enzymatically harvested and grown in tissue culture. After 3 weeks vascular delay and 4 weeks electrical conditioning, 5 SMVs were seeded with 5-8x10<sup>6</sup> autologous endothelial cells by percutaneous injection of a cellular suspension in 5 ml of culture media into the SMV lumen; one SMV was injected with culture media alone as an unseeded control. The autologous endothelial cells were all prelabeled with a lipid-bound cellular marker, PKH-26. After an additional 4 weeks of electrical conditioning, the mandrels were removed and the SMVs connected to the descending thoracic aorta and activated to contract during cardiac



diastole at a 1:2 ratio with the heart. After 3 hours of continuous pumping, mean diastolic pressure was increased by 35% ( $58 \pm 7$  vs  $78 \pm 6$  mmHg,  $p < 0.05$ ). The SMVs were excised for histologic examination. Hematoxylin and eosin (H&E) stained sections revealed a continuous cellular layer lining 50-80% of the SMVs; there were no cells present on the lumen of the control SMV. All seeded SMVs exhibited fluorescence secondary to the PKH-26 cellular marker. Immunofluorescent staining with antibodies to von Willebrand factor and ultrastructural analysis with electron microscopy confirmed the endothelial character of these cells lining the lumen of the SMVs. To our knowledge, this is the first time that an endothelial cell seeded, cardiac assist device has retained endothelium while functioning effectively in the circulation. This is not only another major step towards the clinical application of SMVs, but it also holds enormous implications for the resolution of thrombotic events in mechanical cardiac assist devices as well.

\*By invitation

#### **F18. THE ALLOGRAFT VALVE IN AORTIC VALVE REPLACEMENT AND IN TRANSPLANTED PATIENTS**

Joao Q. Melo, M.D., Ph.D.\*, Jose P. Neves, M.D.\*, Sancia Ramos, M.D.\*, Ana P. Martins, M.D.\*, Narciso C. Andrade, M.D.\* and Manuel M. Macedo, M.D., Ph.D.

*Carnaxide and Lisbon, Portugal*

Clinical behaviour of aortic allograft valves is different in aortic valve replacement (AYR) and in heart transplanted (HT) patients. The study of post-mortem and explanted specimens is crucial for the understanding of its biology. We have used histology, immunohistochemistry and DNA individual profiles to assess 10 aortic valves after AYR (5) or HT (5). Genetic profiles were characterized using di-nucleotide repeats. DNA extracted from different portions of each cusp was PCR amplified using fluochrome labelled primers and analyzed in a ABI gene scanner.

In the AYR group, 4 allograft valves were cryopreserved and 1 was fresh. The cryopreserved valves had no warm ischemic time and the cold ischemic time was 36 to 48 hours. Three allografts explanted before 6 months had a 66% reduction of fibroblasts and the 2 with more than 6 months of implantation were acellular. In 2 allografts T lymphocytes were identified in the leaflets.

The 5 aortic valves of HT patients were obtained from patients who died 1 to 47 months after heart transplantation. These aortic valves had normal morphology and the only histologic abnormal feature was a slightly reduced number of fibroblasts on the free edge of the cusps. In the HT valves, the fibroblasts in the central portion of each leaflet had DNA profile from the donor and at the base of the cusp there were cells from the donor and from the receiver.

These findings favor the concept that allografts are antigenic and immunosuppression may play a role on its long term function.

\*By invitation

### **WEDNESDAY MORNING, APRIL 27, 1994**

#### **9:00 a.m. SIMULTANEOUS SCIENTIFIC SESSION D - ADULT CARDIAC SURGERY**

**East Ballroom**

**Moderators: John A. Waldhausen, M.D.**

**Mortimer J. Buckley, M.D.**

#### **39. PATHOGENESIS OF ACUTE ISCHEMIC MITRAL REGURGITATION IN THREE-DIMENSIONS**

Robert C. Gorman, M.D.\*, James S. McCaughan, M.D.\*, Mark B. Ratcliffe, M.D.\*,  
Krishanu B. Gupta, Ph.D.\*, James T. Streicher, Ph.D.\*, Victor A. Ferarri, M.D.\*,  
Martin St. John-Sutton, M.D.\*, Daniel K. Bogen, Ph.D., M.D.\* and L. Henry  
Edmunds, Jr., M.D.

*Philadelphia, Pennsylvania and San Francisco, California*

Repair of acute ischemic mitral regurgitation (MR) is compromised by ignorance of the mechanism by which a structurally normal valve becomes incompetent. We postulate that acute changes in annular circumference and cross-sectional area and in the dynamics and distances between mitral subunits and infarcted ventricle cause acute MR.

In 22 anesthetized sheep, sonomicrometry transducers were placed on the tips and bases of each papillary muscle (n=4) and five transducers were placed around the mitral annulus. These nine transducers continuously generated a total of 36 inter-transducer distances throughout the cardiac cycle, and defined the interrelationships of transducer-tagged mitral valve subunits in 3-D space.

Two weeks later, eight surviving sheep were re-anesthetized and a Millar catheter was inserted retrograde into the LV. Color flow Doppler echo-cardiograms confirmed the absence of MR. Multiple sets of sono-micrometry inter-transducer distances were obtained of the normal mitral valve. Previously placed snares around the second, third and PDA branches of the circumflex coronary artery were tightened to produce a  $40.4 \pm 7.2\%$  infarction of the LV mass and acute 3 or 4+ MR by Doppler echocardiogram. One to four repeat sets of inter-transducer distances were obtained for the regurgitant valve at LV end-diastolic pressures between 11 and 29 mmHg.

Some new observations of the normal valve indicate that annular circumference decreases  $4.6 \pm 1.8$  mm ( $4.5 \pm 1.7\%$ ) with atrial contraction and decreases an additional  $2.2 \pm 1.4$  mm ( $2.1 \pm .9\%$ ) during early LV systole. The posterior papillary muscle (PPM) lengthens  $0.2 \pm 0.14$  mm ( $1.2 \pm .5\%$ ) during isovolumic systole and then shortens  $2.3 \pm 1.3$  mm ( $12.1 \pm 4.1\%$ ) during ejection. After infarction, the PPM paradoxically lengthens instead of shortens throughout systole, and the transcavity distance at ES increases  $5.3 \pm 1.8$  mm ( $24.3 \pm 8\%$ ). End-systolic (ES) annular circumference and area increase  $12.3 \pm 2.5$  mm ( $13.6 \pm 3.1\%$ ) and  $150 \pm 49$  mm<sup>2</sup> ( $31 \pm 9\%$ ).

We conclude that acute annular dilatation, loss of PPM shortening and LV dilatation after massive posterior infarction distort coaptation of the mitral leaflets to produce MR of the structurally normal valve. These data provide a basis for developing improved reparative operations.

\*By invitation

#### **40. AORTIC ROOT REPLACEMENT: RISK FACTOR ANALYSIS OF A SEVENTEEN YEAR EXPERIENCE WITH 259 PATIENTS**

Vincent L. Gott, M.D., A. Marc Gillinov, M.D.\*, Reed E. Pyeritz, M.D.\*, Duke E. Cameron, M.D.\*, Robert L. Ferris, B.A.\*, Bruce A. Reitz, M.D., Peter S. Greene, M.D.\*, Christopher D. Stone, M.D.\* and Victor A. McKusick, M.D.\*

*Baltimore, Maryland; Allegheny, Pennsylvania and Palo Alto, California*

The results of aortic root replacement were examined to determine operative risk and late results of treatment of ascending aortic disease. Between 1976 and 1993, 259 patients (pts) underwent 265 aortic root replacements. The most common indications for operation were

aneurysm (232 pts; 90%) and dissection (26; 10%). Forty three procedures (16%) were performed emergently. Marfan syndrome was present in 188 (73%), reflecting a referral pattern of our institution. Compared to other pts, Marfan pts were less likely to have dissection ( $p<.009$ ) and emergent operation ( $p<.1$ ). Mean pt age was 38 years (range 4-77) and mean aortic diameter was 7 cm (range 4-16). Root prostheses used were St. Jude composite grafts in 174 pts (66%), Bjork-Shiley in 79 (30%), and cryopreserved homografts in 12 (4%). Hospital mortality occurred in 13 pts (5%); mortality was 1.1% in 188 Marfan pts. Risk factors for death were older age ( $p<.02$ ), preoperative NYHA class III or IV ( $p<.001$ ), acute dissection ( $p<.02$ ), emergent operation ( $p<.001$ ), and use of hypothermic circulatory arrest ( $p<.008$ ). Late follow-up data were available in 95% of hospital survivors. At mean follow-up of 47 months, there have been 22 late deaths; 4 were due to rupture of the distal aorta. Five and 10 year actuarial survival were 90% and 79%, respectively. Fourteen pts (6%) developed endocarditis; 8 died and 4 underwent root re-replacement with aortic homografts without mortality or recurrent endocarditis. Actuarial freedom from reoperation on the aortic root was 96% at 5 years and 88% at 10 years, while freedom from distal aortic surgery was 94% at 5 years and 87% at 10 years. These results demonstrate that aortic root replacement in the current era carries low operative risk, low late mortality and morbidity, and good freedom from reoperation. Endocarditis was the most frequent late complication and was optimally treated by antibiotic therapy and root re-replacement using cryopreserved homograft.

\*By invitation

#### **41. LONG TERM FOLLOW-UP OF PULMONARY VALVE INSERTION: COMPARISON OF ISOLATED PORCINE VALVES, HOMOGRAFTS AND PORCINE VALVED CONDUITS**

Alon S. Aharon, M.D.\* , Hillel Laks, M.D., Davis C. Drinkwater, M.D.\* , Peter Grant,  
M.D.\* , Greg Fontana, M.D.\* , Ehud Rudis, M.D.\* and Mohammed Qureshi, M.D.\*

*Los Angeles, California*

There continues to be uncertainty regarding the optimal valve type to be placed in the right ventricular outflow tract. The results of pulmonary valve replacement using isolated porcine valves (PV), homografts (H), and porcine valved conduits (PC) were compared. Ninety-six children ranging in age from 10 days to 17 years (mean 6 years) and 35 adults ranging in age from 18 years to 74 years (mean 36 years) underwent 163 pulmonary valve replacement operations from July 1978 to November 1993. In children 77 H (57 aortic homografts and 20 pulmonic homografts), 28 PV, and 23 PC were placed. Insertion of a pulmonary valve was part of the primary procedure in 98/128 (77%) operations in children with the following diagnoses: TOP (27), PA-VSD (27), truncus arteriosus (18), TGA-VSD-PS (13), PA-IVS (4), corrected TGA-VSD-PS (4), PS (3), and others (2). Thirty children underwent redo procedures for obstructed pulmonary valves with the diagnoses of: truncus arteriosus (11), TGA-VSD-PS (8), PA-VSD (3), TOP (3), PA-IVS (3) and others (2). In adults 17 H, 16 PV and 2 PC were placed. Insertion of a pulmonary valve was a primary procedure in 30/35 (86%) with the following diagnoses: TOP (13), PA-VSD (6), PS (6), PI (3) and others (2). There was no early mortality, 1 late death and no valve failures in the adult patients with a mean follow-up of 4 years (range 1 month to 15 years). In the pediatric group there were 5 early (4%) and 3 late deaths (2%) and none of the deaths were related to valve failure. Follow-up was available from 1-14 years (mean 4 years) and 14% of children were reoperated on for valve failure at 4 years. In children, actuarial freedom from valve failure using Cox regression analysis (fig. 1) revealed increasing

valve size to be the only significant factor predictive of improved freedom from valve failure ( $p < 0.001$ ). For a given age a significantly larger (4 mm) PV was used when compared to PC and H ( $p < 0.01$ ). Cox regression analysis (fig. 2) also demonstrated that PV showed a trend toward improved freedom from valve failure when compared to H and PC ( $p < 0.06$ ). Freedom from reoperation at 4 years was 100% for PV, 85% for PC and 82% for H.

Conclusion: (1) Larger pulmonary valves offer greater freedom from reoperation. (2) Larger PV can be placed for a given age when compared to PC and H thus conferring greater freedom from reoperation.

\*By invitation

#### **42. TRICUSPID VALVE REPLACEMENT: FIFTEEN YEARS OF EXPERIENCE WITH MECHANICAL AND BIOPROSTHESES**

Hugh E. Scully, M.D., Cathy Tong, H.R.A.\* and Susan Armstrong, M.Sc.\*

*Toronto, Ontario, Canada*

Tricuspid valve replacement is not a common operation. The purpose of this study is to examine the early and late results in 61 patients undergoing 33 (54%) mechanical and 28 (46%) bioprosthetic tricuspid valve replacements. All operations took place between January 1978 and June 1993 when a total of 4741 patients underwent valve replacement surgery.

Mean patient age was  $50 \pm 17$  (18-75) years. 42 pts (69%) were female; 19 pts (31%) were male. 49 pts (80%) were in NYHA Class III or IV pre-operatively. 43 pts (70%) were undergoing redo cardiac valve surgery. 13 pts (21%) had complex congenital cardiac problems. Surgery was urgent in 16 pts (26%). Hospital mortality was 26% (16 pts) - all NYHA Class III or IV, redos and/or complex congenital cases. Low output syndrome was observed in 21 pts (41%). Reoperation for bleeding was required in 8 pts (13%). 19 pts (31%) required permanent (epicardial lead) pacemaker implantation.

Mean follow-up is 69 months (max. 170) and is 100% complete for the 45 patients who left hospital. There have been 13 late deaths (21%). 9 of these pts (69%) had mechanical valves and 4 pts (31%) had bioprostheses. Of the 9 cardiac deaths, 2 were valve-related (bioprostheses). 3 pts (7%) of the 32 still surviving required re-operation because of TV prosthetic failure (one thrombosed mechanical, 2 failed porcine). Of the remaining 29 patients, 10 (66%) are in NYHA Class I or II. 16 pts have mechanical and 13 pts bioprostheses. 25 pts (86%) are on coumadin. Thromboembolism (transient TIA) has occurred in 1 pt with a mechanical valve who also had a previous CVA. There has been no haemorrhage, endocarditis or new pacemaker requirement. Actuarial survival for the series is  $39 \pm 8\%$  at 15 years. Freedom from valve-related complications among the 45 hospital survivors is  $76 \pm 9\%$ .

Tricuspid valve replacement is a beneficial procedure for patients with structural tricuspid valve disease, many of whom have other valvular or congenital disease. Mechanical and bioprostheses are equally effective in the tricuspid position.

#### **10:20 a.m. INTERMISSION**

\*By invitation

## 11:05 a.m. SIMULTANEOUS SCIENTIFIC SESSION D - ADULT CARDIAC SURGERY

### East Ballroom

Moderators: John A. Waldhausen, M.D.

Mortimer J. Buckley, M.D.

#### 43. MYECTOMY FOR HOCM: EARLY AND LATE RESULTS

Elaine Heric, M.D.\*, Bruce W. Lytle, M.D, Eliot R. Rosenkranz, M.D.\*, Harry M.

Lever, M.D.\* and Delos M. Cosgrove, M.D.

*Tacoma, Washington and Cleveland, Ohio*

From 1975 through 1993 178 patients underwent surgical management of hypertrophic obstructive cardiomyopathy (HOCM). Operations included isolated septal myectomy (SM), 96, SM and coronary artery bypass grafting (CABG), 41, SM plus a valve procedure, 24, SM, valve and CABG, 14, and mitral valve replacement (MVR) without SM, 3. Recent myectomy results were monitored by transesophageal echocardiography. After initial myectomy 32 patients (20%) underwent a second pump run for more extensive myectomy only (22), MVR only (7) or both (2). In-hospital mortality was 11 (6%), 6 (4%) patients undergoing SM or SM plus CABG. Heart block occurred in 18 patients (10%). Left ventricular outflow tract systolic gradients decreased from a mean of 93 mmHg to 21 mmHg post myectomy.

Late survival was 86% and 70% at 5 and 10 postoperative years, respectively, 93% and 79% for patients undergoing SM alone or SM plus CABG. Only 3 of 131 in-hospital survivors of SM or SM plus CABG died late cardiac deaths, for a yearly mortality of .6%. However, the 5-year late survival of patients undergoing valve operation plus SM was 51% and multivariate testing confirmed that adverse influence on late survival ( $p=0.01$ ), as well as adverse influences of increasing age ( $p=0.023$ ) and return to cardiopulmonary bypass for further procedures ( $p=0.027$ ). At follow-up 94% (136) of patients had NYHA I or II symptoms.

For patients with HOCM, SM alone or in combination with CABG produces effective symptom relief, excellent long-term survival and a low risk of late cardiac death.

\*By invitation

#### 44. EXPERIENCE WITH THE WEARABLE NOVACOR LEFT VENTRICULAR ASSIST SYSTEM AS A BRIDGE TO CARDIAC TRANSPLANTATION

Herbert O. Vetter, M.D.\*, Hans G. Kaulbach, M.D.\*, Eckart Kreuzer, M.D.\*,

Christoph Schmitz, M.D.\*, Hermann Reichenspurner, M.D., Ph.D.\* and Bruno

Reichart, M.D.\*

*Munich, Germany*

*Sponsored by: R.W.M. Prater, M.D., Bronx, New York*

The three components of the Novacor left ventricular assist system (LVAS) - compact controller, battery, and back-up battery - have been miniaturised in the development of the wearable system. Therefore, patients (pts) can be mobilized almost completely during mechanical circulatory support (MCS) while awaiting heart transplantation (HTx).

Between 2/92 and 10/93 a total of 8 pts suffering from decompensated heart failure (4 dilated cardiomyopathy, 3 ischemic heart disease, 1 acute myocarditis, 1 postcardiotomy) were treated with the Novacor LVAS; the last 4 cases using the wearable system N100P. The pts age ranged from 17 to 59 years. In 6 pts severe right heart failure was present at the time of implantation. Heparin IV was used for anticoagulation treatment followed by oral phenprocoumon combined with low dose acetylsalicyl acid.

Hemodynamic stabilisation could be achieved in all pts during the 2 to 50 days (mean  $15 \pm 19$  days) of MCS. One pt is supported at present and treated for legionellosis of the lungs since more than 4 weeks. The following parameters were measured before and 24 hrs after LVAS implantation: mean arterial pressure  $67 \pm 7$  vs.  $90 \pm 13$  mmHg ( $p < 0.05$ ), cardiac index  $1.69 \pm .43$  vs  $3.17 \pm .80$  l/min/m<sup>2</sup> ( $p < 0.01$ ), mean pulmonary artery pressure  $40 \pm 9$  vs  $25 \pm 8$  mmHg ( $p < 0.05$ ), pulmonary capillary wedge pressure  $25.1 \pm 4.4$  vs  $9.6 \pm 5.8$  mmHg ( $p < 0.05$ ). Right ventricular ejection fraction (RVEF), measured by a rapid response thermodilution catheter, improved during left ventricular support in pts with global heart failure; RVEF before LVAS implantation  $13.2 \pm 10.7\%$  to  $24.3 \pm 13.9\%$  at the time of HTx. The postcardiotomy pt died from multi-organ failure. In 6 pts a HTx could be performed; 1 pt died due to unspecific graft failure. 5 pts are rehabilitated and 4 of them have returned to work. Pts on the wearable system were able to manage their own power supply and power care during MCS allowing them to walk in the hospital garden to go to the shopping area.

The new wearable Novacor LVAS provides major advantages regarding "quality of life" of pts during MCS.

\*By invitation

#### **45. RETROGRADE CEREBRAL PERFUSION DURING HYPOTHERMIC CIRCULATORY ARREST REDUCES NEUROLOGIC MORBIDITY**

G. Michael Deeb, M.D., Steven F. Bolling, M.D., Louis A. Brunsting, M.D.\*, David M. Williams, M.D.\*, Leslie E. Quint, M.D.\* and Nancy D. Deeb, R.N.\*

*Ann Arbor, Michigan*

Hypothermia circulatory arrest (HCA) has become an accepted technique for a variety of cardiac and complex aortic operations. However, prolonged periods (>45 min) of HCA in older patients is associated with marginal cerebral protection and an increased incidence of adverse neurologic events. In an effort to minimize such morbidity, we employed a technique of retrograde cerebral perfusion (RCP) during HCA in 16 patients who underwent thoracic aortic surgery or resection of intracardiac tumor. There were 12 males and 4 females (mean age 62, range 36-76). Six patients presented with acute dissection, 8 had thoracic aortic aneurysms, and 2 with hypernephromas extending into the heart. Ten patients underwent root and arch replacement utilizing composite grafts (3 with simultaneous coronary artery bypass grafting), 4 had arch replacement, and 2 resection of tumor in the heart and retrohepatic vena cava. Ten cases were elective and 6 emergent, 4 (25%) were reoperations.

Operative technique included a median sternotomy, cardiopulmonary bypass (CPB) using common femoral arterial perfusion (CFAP) and right atrial venous drainage, retrograde cardioplegia, and venting of the left ventricle. RCP was accomplished during HCA using a right angled cannula in the superior vena cava (SVC), Y-connected into the arterial perfusion line. When the core temperature was  $< 20^{\circ}\text{C}$ , CFAP was discontinued and RCP was instituted to maintain a perfusion pressure in the SVC  $< 15$  mm/Hg. RCP flows varied from 350-800 ml/min. CPB suckers

were used to return RCP flow. After completion of the surgical procedure, RCP was halted and CFAP resumed.

The mean RCP time was  $57 \pm 4$  min (range 35-96 min), with 13 (81%) patients  $>45$  min. There was one operative death and 1 late death, both due to pre-op myocardial infarction from aortic dissection. One patient had a stroke secondary to acute dissection of the left carotid artery. There were no other neurologic events, re-operations for bleeding or adverse outcomes. The average length of stay for elective cases was 9 days and for emergent cases 28 days. At a mean follow up of 5 months all surviving patients are well.

HCA is a relatively simple technique which provides a bloodless field and good visualization without the need for aortic cross clamps. Moreover, RCP extends the "safe" time for HCA allowing ample opportunity to perform complicated cardiac and aortic surgery with reduced risk of adverse neurologic events.

**12:00 p.m. ADJOURN**

\*By invitation

### **WEDNESDAY MORNING, APRIL 27, 1994**

#### **9:00 a.m. SIMULTANEOUS SCIENTIFIC SESSION E - GENERAL THORACIC SURGERY**

**Trianon Ballroom**

**Moderators: Andre C.H. Duranceau, M.D.**

**Willard A. Fry, M.D.**

#### **46. PULMONARY RESECTION FOR INVASIVE ASPERGILLUS INFECTIONS IN IMMUNOCOMPROMISED PATIENTS**

Lary A. Robinson, M.D.\*, Elizabeth C. Reed, M.D.\*, Timothy A. Galbraith, M.D.\*, Anselmo Alonso, M.D.\*, Anthony L. Moulton, M.D. and William H. Fleming, M.D.

*Omaha, Nebraska and Providence, Rhode Island*

Standard medical therapy of invasive pulmonary aspergillus infections occurring after bone marrow transplantation (BMT) or liver transplantation (LT) results in less than a 5% survival. Therefore, we adopted an aggressive approach with surgical resection of the involved area along with systemic antifungal therapy when a localized pulmonary aspergillus infection develops in these severely immunocompromised patients.

**METHODS:** from May 1987 TO October 1993, 12 (BMT) and 3 (LT) patients underwent resection of localized acute pulmonary masses suspicious for invasive aspergillus, as suggested by chest CT scans and clinical signs and symptoms. Operative procedures performed include 2 pneumonectomies, 1 bilobectomy with limited thoracoplasty, 8 lobectomies, and 5 wedge resections (one BMT patient had two procedures). All patients were also treated with systemic antifungal agents. The diagnosis of invasive pulmonary aspergillus infection was confirmed by characteristic histopathology and/or positive cultures.

**RESULTS:** 8 of 12 (67%) BMT patients and 2 of 3 (67%) LT patients survived the perioperative period with no evidence of recurrent aspergillus infection. Despite the severe pyrexia present in most patients, none had positive blood cultures for aspergillus nor any other evidence of disseminated disease. Five hospital deaths (4 BMT, 1 LT) occurred a mean  $22.4 \pm 12.4$  days after surgery from continuing systemic toxicity and multiple organ failure. Both ventilator-dependent

patients in the series died. In addition, 3 of the 4 deaths in BMT patients occurred in allogeneic BMT recipients.

Of survivors, no surgical complications occurred post-operatively except for renal insufficiency that was felt related to amphotericin B. Surgery on BMT patients was performed a mean  $37.4 \pm 16.0$  days after starting initial high dose chemotherapy. Two LT patients underwent their resection 9 and 48 days after transplant. Surgery was performed in the other LT patient 7 days after starting medical treatment for an acute rejection episode. The 10 initial survivors (8 BMT and 2 LT) were followed for a mean  $16.3 \pm 24.8$  months (range 0.25-78) months. Four BMT patients have subsequently died from progression of their malignancy, but none developed a recurrent aspergillus infection.

CONCLUSIONS: 1) Immunocompromised BMT and LT patients who develop the uniformly fatal complication of invasive pulmonary aspergillus infections may benefit from early surgical resection of the involved area, with 2/3 of such patients in this series cured of their fungal infection long term. 2) Ventilator dependent patients, allogeneic BMT recipients, and patients with multiple loci of infection are less likely to benefit from this approach. 3) Early pulmonary resection with lobectomy or occasionally wedge resection for smaller lesions should be performed when the characteristic clinical and radiographic pictures appear, and should not await positive cultures or a trial of antifungal chemotherapy.

\*By invitation

#### **47. OUTCOME OF ADENOCARCINOMA ARISING IN BARRETT'S ESOPHAGUS IN ENDOSCOPICALLY SURVEYED AND NON-SURVEYED PATIENTS**

Geoffrey W.B. Clark, F.R.C.S.(Ed)\*, Adrian P. Ireland, F.R.C.S.(I)\*, Jeffrey H. Peters, M.D.\*, Thomas C. Smyrk, M.D.\*, Para Chandrasoma, M.D.\* and Tom R. DeMeester, M.D.

*Los Angeles, California and Omaha, Nebraska*

The value of endoscopic surveillance of Barrett's esophagus and the appropriate management of high grade dysplasia (HGD) remains unclear. Recent reports have proposed that endoscopy and biopsy can accurately differentiate HGD from intramucosal adenocarcinoma, thus continued surveillance of HGD is safe. The method of surveillance and outcome of treatment in patients with severe dysplasia or adenocarcinoma arising in Barrett's esophagus was evaluated to address these uncertainties.

The study population consisted of 16 patients referred from endoscopic surveillance programs, 11 with HGD and 5 with adenocarcinoma, and 33 patients with a newly recognized adenocarcinoma who were not under surveillance. The flow chart shows the subsequent outcome of those patients referred from surveillance. Following repeat endoscopy with extensive biopsy, 2 were diagnosed as adenocarcinoma while 9 were operated with a diagnosis of HGD. In 7 of these 9 patients no mucosal abnormality was seen endoscopically while one had stricture and one a small superficial ulcer.

The median number of biopsies taken was 15 (range 7-34). The median number of biopsies per cm of Barrett's was 3.9 (range 0.8-7.5). Tumors were staged post operatively by the WNM classification based on the degree of wall penetration and the number of lymph node metastasis. Despite the high number of biopsies per cm 5 patients with adenocarcinoma were missed. Twelve patients in the screened group had adenocarcinoma: 11 early and 1 intermediate. Patients not under surveillance presented with more advanced tumors: 11 early, 9 intermediate and 13 late ( $X^2=12.2$ ,



p<0.01). Sixteen patients referred from surveillance, despite the presence of adenocarcinoma in 12, enjoyed a significantly improved survival compared to the non surveyed group (X<sup>2</sup>=4.2, p<0.05).

Patients referred from surveillance programs for Barrett's esophagus have a better outcome and earlier stage tumors compared to non surveyed patients. Multiple biopsies do not exclude the presence of adenocarcinoma making continued surveillance of high grade dysplasia dangerous and potentially destructive to surveillance efforts.

\*By invitation

#### **48. p53 IMMUNOREACTIVITY IN BARRETT'S METAPLASIA, DYSPLASIA AND CARCINOMA**

Thomas W. Rice, M.D., John R. Goldblum, M.D.\*, Gary W. Falk, M.D.\*, Raymond

R. Tubbs, M.D.\*, Thomas J. Kirby, M.D.\* and Graham Casey, M.D.\*

*Cleveland, Ohio*

Mutations of the tumor suppressor gene p53 frequently result in intranuclear protein accumulation and are implicated in the loss of regulation of normal cell growth and differentiation. Barrett's esophagus is a metaplastic condition with an unpredictable potential for neoplasia. The study was undertaken to determine 1) if the expression of p53 in Barrett's esophagus is a marker for neoplasia and 2) when in the metaplasia-dysplasia-carcinoma sequence p53 expression occurs.

Twenty-eight esophageal resection specimens were studied. In each specimen (28) Barrett's mucosa (BM) was present. Low grade dysplasia (LGD) was seen in 27 specimens, high grade dysplasia (HGD) in 26, intramucosal cancer (IMC) in 18, and submucosal cancer (SMC) in 5. Immunohistochemical staining with the monoclonal antibody PAbISO1 was used to detect mutated intranuclear p53.

No p53 immunoreactivity was seen in BM or LGD. p53 was seen only in HGD, IMC, and SMC. Sixty-nine percent (18/26) of these specimens expressed p53. In those specimens in which p53 staining was observed, the spectrum of neoplastic changes (HGD, IMC, SMC) within the specimen was positive for p53. Of the 8 specimens where the most severe neoplastic change was HGD, 6 (75%) expressed p53 immunoreactivity. Similarly, 10 of 13 IMC (77%) and 2 of 5 SMC (40%) expressed p53 immunoreactivity.

We conclude that p53 immunoreactivity in Barrett's esophagus 1) is a frequent, but not exclusive, marker for HGD, IMC, and SMC and 2) occurs late in the metaplasia-dysplasia-carcinoma sequence when HGD transformation has occurred.

\*By invitation

#### **49. CARCINOMA OF THE ESOPHAGUS: PROGNOSTIC SIGNIFICANCE OF HISTOLOGY**

Michael D. Lieberman, M.D.\*, Craig D. Shriver, M.D.\*, Steven Bleckner, B.S.\*,

Michael Burt, M.D., Ph.D. and the members of the Thoracic and Gastric and Mixed

Tumor Services

*New York, New York*

**Introduction:** Previous investigators have suggested that adenocarcinoma of the esophagus when compared to squamous cell carcinoma adversely affects prognosis. A review of 258 patients, from 1985-1991, undergoing esophagectomy for adenocarcinoma or squamous cell carcinoma was performed to test the hypothesis that histology is an independent prognostic variable, and to identify other predictors of survival following esophagectomy.

**Methods:** Seventeen demographic, clinical, treatment and pathologic variables were analyzed for effect on overall and disease free survival following curative esophageal resection. The primary operative procedures were transthoracic esophagectomy (79%), transabdominal esophago-gastrectomy (9%), transhiatal esophagectomy (7%) and pharyngo-esophagectomy (5%). The median followup was 18 mos. The in-hospital mortality was 5%. Univariate analysis of survival for each variable was determined by the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model.

**Results:** The median overall survival was 27 mos. for adenocarcinoma compared to 22 mos. for squamous cell,  $p=0.16$  (figure). Univariate analysis identified T stage, N stage, number of positive nodes, tumor differentiation, tumor site and blood transfusion as significant ( $p<0.05$ ) variables in predicting overall survival. Age, sex, dysphagia, tobacco use, alcohol use, weight loss, Barrett's esophagus, operative procedure, margins, splenectomy, and anastomotic leak were not significant prognostic factors. The table indicates prognostic factors derived from the Cox model, and the figure demonstrates overall survival according to histology.

Cox Multivariate Analysis

<u>Characteristic</u>	<u>Overall Survival (p)</u>	<u>3-Yr Overall Surv (%)</u>
TNM: T stage	0.006	T1=64, T2=56, T3=30
TNM: N stage	0.01	N0=56, N1=27
No. of Pos. Nodes	0.03	0=56, 1-3=37, >3=18
Blood Transfusion	0.07	No=47, Yes=31

Histology, tumor location, tumor differentiation, microscopic margin, splenectomy, preoperative weight loss and age were not significant variables in the Cox model.

**Conclusion:** Multivariate analysis demonstrated that histology is not an independent variable for overall survival in patients undergoing curative resection of esophageal carcinoma. Outcome following curative esophagectomy is most strongly influenced by extent of disease defined by T and N stage.

**10:20 a.m. INTERMISSION**

\*By invitation

**11:05 a.m. SIMULTANEOUS SCIENTIFIC SESSION E - GENERAL THORACIC SURGERY**

**Trianon Ballroom**

**Moderators: Andre C.H. Duranceau**

**Willard A. Fry, M.D.**

**50. TREATMENT STRATEGIES FOR BRONCHOPLEURAL FISTULA**

John D. Puskas, M.D.\*, Douglas J. Mathisen, M.D., Hermes C. Grille, M.D., John C.

Wain, M.D.\*, Cameron D. Wright, M.D.\* and Ashby C. Moncure, M.D.

*Boston, Massachusetts*

Successful management of chronic bronchopleural fistula (BPF) remains a challenge for thoracic surgeons. Forty-seven patients were treated for postoperative BPF since 1978. Patients had undergone an average of 3.1 surgical procedures to correct their BPFs during a mean interval of 24 months prior to our treatment. BPFs were located in the right main bronchial stump (22), right lobar bronchial stumps (12), left main bronchial stump (8), left lobar stump (1), trachea (2) and parenchyma (2). Patients were treated by suture closure of the bronchial stump in 37, buttressed with vascularized pedicle flaps of omentum (19), muscle (14), or pleura (3). In 10 cases, direct suture closure was not possible, and omental (7) or muscle (2) flaps were sutured over the BPF. Suture closure without pedicle coverage and simple drainage were performed successfully in one case each. Initial repair of BPF was successful in 21 of 26 patients treated with omentum, in 11 of 16 patients treated with muscle and in 1 of 3 patients treated with pleural flaps. In 12 patients with persistent or recurrent BPF after our initial repair, 7 underwent a second procedure (5 successful) and 5 were managed with drainage only. BPF was successfully closed in 11 of 13 patients who had received high-dose radiation therapy (9 with omentum). Overall, successful closure of BPF was achieved in 40 of 47 patients (85%). Four in-hospital deaths resulted from pneumonia and sepsis, 2 in patients with recurrent BPF after pleural flap closure. In 25 patients, the empyema cavity was obliterated during definitive repair of the BPF. The cavity resolved with drainage in 6 others, while 10 required a total of 17 Clagett procedures and 1 had a delayed myoplasty. Direct surgical repair of chronic BPF may be achieved in most patients after adequate pleural drainage by suture closure and aggressive transposition of vascularized pedicle flaps. Omentum is particularly effective in buttressing the closure of BPF.

\*By invitation

## **51. PROGNOSIS AND MANAGEMENT OF MELANOMA PATIENTS WITH PULMONARY METASTASES**

Lorraine Tafra, M.D.\*, Paul S. Dale, M.D.\*, Leslie A. Wanek, Dr.P.H.\* and Donald L. Morton, M.D.

*Santa Monica, California*

Although melanoma that metastasizes to distant sites is generally associated with a median survival of only 6 to 8 months, certain metastatic sites including the lung may carry a better prognosis than others. Surgical therapy of pulmonary metastases remains controversial because of the variable survival rates reported for previous small series. To determine the prognosis and optimal management of melanoma patients with pulmonary metastases, we reviewed our 21-year melanoma database of over 6,000 patients. Of 953 AJCC stage IV patients with metastatic melanoma involving the lung, 100 underwent surgical resection by unilateral/bilateral thoracotomy or median sternotomy. Operative mortality was zero and median follow-up was 61 months. The remaining 853 patients were managed nonsurgically by immunotherapy, chemotherapy and/or radiation therapy. In both treatment groups the male:female ratio was similar (approximately 2:1). The primary lesion's Clark level of invasion and Breslow thickness, and the patient's age at initial diagnosis and diagnosis of stage IV disease were not significantly different between the two groups. Fifty-nine percent of the nonsurgical group developed extrathoracic metastases, compared to 38% of the surgical group ( $p < .001$ ). The 1-year, 3-year and 5-year survival rates of surgical patients

were 77%, 34% and 28%, respectively, compared to 32%, 7% and 3% in nonsurgical patients; these differences were highly significant (p<.001). Sixty-eight percent of the surgical patients received some form of immunotherapy, compared to 39% of the nonsurgical patients. Multivariate analysis revealed that both surgery and immunotherapy were independent predictors of survival (p<.0001). These results indicate that the prognosis associated with metastatic melanoma may be less dismal when distant disease involves thoracic sites. We believe that surgical resection is the treatment of choice for melanoma patients with pulmonary metastases; when combined with immunotherapy, this regimen offers the best chance for long-term survival.

\*By invitation

**52. RESULTS OF CALGB 8935: A MULTI-INSTITUTIONAL PHASE II TRI-MODALITY TRIAL FOR STAGE IIIA (N2) NON-SMALL CELL LUNG CANCER (NSCLC)**

David J. Sugarbaker, M.D.\* , James E. Herndon\* , Leslie J. Kohman, M.D.\* , Hani Shennib, M.D.\* , William C. Nugent, M.D.\* , Mark Krasna, M.D.\* , Jemi Olak, M.D.\* , Carolyn M. Dresler, M.D.\* , Mark K. Ferguson, M.D. , Carolyn E. Reed, M.D.\* , Frederic C. Kass, M.D.\* , Parvesh Kumar, M.D.\* , Michael T. Jaklitsch, M.D.\* , Michael A. Maddaus, M.D.\* , Nasser K. Altorki, M.D.\* and Mark R. Green, M.D.\*

*Boston, Massachusetts; Durham, North Carolina; Syracuse and New York, New York; Montreal, Quebec, Canada; Dartmouth, New Hampshire; Baltimore, Maryland; Richmond, Virginia; St. Louis, Missouri; Chicago, Illinois; Charleston, South Carolina; Santa Barbara and San Diego, California; Memphis, Tennessee and Minneapolis, Minnesota*

Thirty institutions participated in CALGB 8935, a phase II tri-modality trial for patients (pts) with stage IIIA (N2) NSCLC. Two cycles of induction cisplatin (P) 100 mg/m<sup>2</sup> and vinblastine (V) 5 mg/m<sup>2</sup>/week preceded standardized resection. Resected pts received two cycles adjuvant P and V followed by 55 Gy radiotherapy (RT). From 10/89 to 2/92, 80 pts were accrued. The age of 74 eligible pts ranged between 45 to 75 yrs. Histology: 43% squam, 35% adeno, 22% undiff. All pts were staged as IIIA by cervical and/or anterior mediastinoscopy; 92% had more than 1 node biopsied and bronchoscopy identified endobronchial tumor in 29%. There were no radiographic complete responses to induction P and V; 65 (88%) had a response or stable disease, 6 (8%) developed distant metastases, and 3 (5%) were unevaluable. Sixty-two (84%) pts underwent thoracotomy, of whom 45/62 (73%) were resectable; 24/45 (53%) had lobectomy, 17/45 (38%) pneumonectomy, 2/45 (4%) sleeve resection, 2/45 (4%) lobectomy with chest wall resection and all had radical lymphadenectomy. Operative mortality was 3.2% (2/62 pts). Postoperative morbidity: pneumonia (9%), dysrhythmia (7%), respiratory failure (3%), bronchopleural fistula (3%), and empyema (2%). Ten pts (22%) were pathologically downstaged at resection; 4/45 (9%) stage II, 6/45 (13%) stage I. Twenty-three of 45 pts underwent complete resection. Twenty-two pts were incompletely resected (7 positive margins, 11 positive highest node sampled, and 4 both). Thirty-one pts of 45 resected (69%) completed adjuvant P and V and RT. Median follow-up of pts currently alive is 23.6 months.

N	PATTERNS OF RECURRENCE				SURVIVAL		
	Local	Distant	Both	None	1 yr	2 yr	3 yr

Eligible	74					64%	33%	19%
<b>Resected</b>	45					65%	43%	36%
Complete	23	4%	39%	9%	48%	68%	42%	42%
Partial	22	0%	27%	32%	41%	63%	44%	29%
Unresectable	17					35%	20%	0%

CALGB 8935 has shown in IIIA (N2) NSCLC: 1) mediastinoscopy, induction chemotherapy, standardized surgical resection, and adjuvant chemo and RT is feasible in a multi-institutional setting, 2) disease progression during induction chemo is uncommon (8%), 3) single modality induction therapy can yield acceptable resectability rates with low operative mortality, 4) resection is associated with improved survival compared to previous studies. These data lay the foundation for future randomized phase III multi-institutional trials to determine the superiority of this approach to single modality therapy.

**12:00 p.m. ADJOURN**

\*By invitation

### **WEDNESDAY MORNING, APRIL 27, 1994**

#### **9:00 a.m. SIMULTANEOUS SCIENTIFIC SESSION F - CONGENITAL HEART DISEASE**

**West Ballroom**

**Moderators: Richard A. Jonas, M.D.**

**Julie A. Swain, M.D.**

#### **53. THE NORWOOD OPERATION AND SUBSEQUENT FONTAN OPERATION IN INFANTS WITH COMPLEX CONGENITAL HEART DISEASE**

Paul W. Weldner, M.D.\* and John L. Myers, M.D.

*Hershey, Pennsylvania*

From April 1987 to September 1993, 60 infants underwent a Norwood operation for complex congenital heart disease including hypoplastic left heart syndrome (HLHS) (n=41), ventricular septal defect (VSD) and subaortic stenosis (SubAS) with arch interruption/severe coarctation (IAA) (n=6), complex single right ventricle (SRV) with SubAS (n=8), critical aortic stenosis with endocardial fibroelastosis (n=3), and malaligned primum atrial septal defect with coarctation (n=2). Age at operation ranged from 1 day to 3.9 months (mean 10.5 days, median 3.5 days).

The overall operative mortality (<30 days) was 30% (20 patients). Late mortality was 17% (10 patients).. Fifteen of the 20 (75%) operative deaths occurred suddenly during the first two days postop from sudden hemodynamic instability. All four infants with premature closure of the foramen ovale had pulmonary lymphangiectasia and died from pulmonary failure. There have been 7 operative deaths in 36 patients since 1990 (19%) and in the last 2 years there have been no operative deaths in 22 patients.

Overall, there are 30 late survivors (50%). Nineteen of these 30 infants have undergone a modified Fontan operation at 9.7 to 27.6 months of age (mean 18.1 months) with no mortality. Another six patients have undergone a hemi-Fontan at 6.8 to 23.0 months (mean 11.7 months) with no mortality. In our early experience, infants undergoing the Norwood operation had a high early mortality, related to sudden hemodynamic instability. Following the institution of a protocol for the addition of CO<sub>2</sub> to the inspired gas during postop mechanical ventilation there has been no

operative deaths. The operative mortality for the Norwood operation continues to improve. Subsequent Fontan operation can be performed with excellent clinical results.

\*By invitation

#### 54. WHAT AFFECTS VENTRICULAR CHARACTERISTICS AFTER A FONTAN TYPE OPERATION?

Hideki Uemura, M.D.\*, Toshikatsu Yagihara, M.D.\*, Yasunaru Kawashima, M.D.,

Fumio Yamamoto, M.D.\*, Osamu Matsuki, M.D.\* and Robert H. Anderson, M.D.\*

*London, England and Osaka, Japan*

Postoperative conditions after a Fontan type operation, particularly as they affect results in the early term, are thought to depend on factors such as the state of the pulmonary circulation and ventricular function, as well as the sequels of the operative procedure. In this study, we have attempted to determine the factors affecting ventricular characteristics in the middle term after Fontan-type procedures.

Postoperative catheterization was performed at a mean of 1.4 years after surgery in 50 patients with univentricular atrioventricular connection who underwent the operation at the age of 1.0-22.6 years. End diastolic volume (EDV: % of anticipated normal value), ejection fraction (EF) and end diastolic pressure (EDP) of the systemic ventricle were analyzed in addition to calculation of the cardiac index (CI).

As shown on the table, these parameters were affected by presence of residual or recurrent atrioventricular valvar regurgitation (AVVR), the morphology of the dominant ventricle [morphologically right (RV) or left ventricle (LV)], the age at the procedure, and the surgical procedure employed [atrio-pulmonary connection (APC) or total cavopulmonary connection (TCPC)]:

	n=	EDV (%)	EF (%)	EDP (mmHg)	CI (l/min/m <sup>2</sup> )
AWR [+]	4	194 ± 56** *	47 ± 14	7.8 ± 1.5 *	1.95 ± 0.22** *
[-]	46	87 ± 22 **	56 ± 12	3.2 ± 2.0**	2.52 ± 0.47**
RV type	23	93 ± 38	49 ± 9**	3.8 ± 2.4	2.63 ± 0.46
LV type	27	99 ± 41	60 ± 4**	3.4 ± 2.3	2.35 ± 0.47
age	40	r=-0.12	r=-0.53*	r=0.05	r=-0.19
APC	24	94 ± 41	54 ± 14	3.3 ± 2.2	2.23 ± 0.34** *
TCPC	26	98 ± 37	54 ± 12	3.9 ± 2.4	2.72 ± 0.48**

(r: correlation coefficient, \*:P<0.01).

The value of correlation coefficient indicates, with statistical significance, that a younger age is associated with a better postoperative ejection fraction. Although it is not easy to define the exact meaning of a good ejection fraction in the Fontan circulation, a better fraction can never be considered to worsen the efficiency of the circulation.

On the basis of our results, therefore, we conclude that an earlier TCPC, if possible, could be the surgical procedure of choice, and that AVVR must be treated properly at definitive repair.

\*By invitation

**55. MIDLINE ONE STAGE COMPLETE UNIFOCALISATION AND REPAIR OF PULMONARY ATRESIA, VENTRICULAR SEPTAL DEFECT, DIMINUTIVE OR ABSENT TRUE PULMONARY ARTERIES, AND MULTIPLE AORTOPULMONARY COLLATERALS**

V. Mohan Reddy, M.D.\* , John R. Liddicoat, M.D.\* and Frank L. Hanley, M.D.\*,  
*San Francisco, California*

*Sponsored by: Benson B. Roe, M.D., San Francisco, California*

Traditionally patients with pulmonary atresia, ventricular septal defect (VSD), diminutive or absent central pulmonary arteries (PA) and multiple aortopulmonary collaterals (MAPCAS) have been managed by staged procedures requiring multiple operations. We have undertaken a new approach to this lesion. Between 8/92 and 11/93, 8 patients aged 2.5 months to 36 years (4 pts < 9 months old) at the severe end of the morphologic spectrum of this lesion underwent a single stage repair through a midline sternotomy approach. All sources of vascular supply to the lungs were unifocalised (8 pts). A valved homograft conduit was inserted from the right ventricle to the reconstructed PAs (8 pts), and the VSD was closed (7 pts). The average size of the true PAs was 2.16mm (1 to 4mm) and they provided vascular supply on average to only one lobe per patient.

Following sternotomy both hilar regions and the descending aorta were extensively dissected and all collaterals were isolated and secured. As many MAPCAS as possible were unifocalised before going on cardiopulmonary bypass. Complete unifocalisation was achieved in all patients using native tissue-to-tissue connections via anastomosis of collaterals to other collaterals and to the native PAs. Only one patient (36 years old) required a non native conduit for peripheral PA reconstruction. The VSD was left open in one patient (5 years old) because of diffuse distal hypoplasia and stenosis of the PAs and the MAPCAS. The post-repair RV/LV pressure ratio (in 7 pts with VSD closure) ranged from 0.3 to 0.6 (mean=0.448). There were no early deaths. Complications were re-exploration for bleeding in one patient and diaphragmatic plication for phrenic nerve palsy in one other patient. One patient was reoperated for pseudo-aneurysm of the central homograft and then again for stenosis of the left lower lobe pulmonary artery. Following this last operation 13 months after her initial repair she died due to a preventable cardiac arrest secondary to pneumothorax. Her RV/LV pressure ratio was 0.56. The patient with open VSD underwent balloon dilation of her unifocalised PAs with a current Qp:Qs of 2:1 and is scheduled for a VSD closure.

We conclude that this approach establishes normal cardiovascular physiology early in life, eliminates the need for multiple systemic to pulmonary artery shunts and avoids the use of prosthetic material, and minimizes the number of operations required. Long term follow up is essential to determine whether this approach will limit the need for further surgery to central homograft conduit changes only.

\*By invitation

## 56. RESULTS OF EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN NEONATES WITH SEPSIS -THE ELSO EXPERIENCE

Dan M. Meyer, M.D.\*, Michael E. Jessen, M.D.\* and the Extracorporeal Life Support Organization

*Dallas, Texas and Ann Arbor, Michigan*

*Sponsored by: W. Steves Ring, M.D., Dallas, Texas*

Use of ECMO for treatment of respiratory failure secondary to sepsis is controversial due to concerns over survival benefit and hemorrhage-related complications. To evaluate the impact of the primary diagnosis of sepsis on outcome, we reviewed data from 6853 neonates in the ELSO registry and defined two groups: Group 1 (n=1060) all patients undergoing ECMO with a primary diagnosis of sepsis and Group 2 (n=5793) those with any other primary diagnosis. A multivariate logistic regression analysis which considered 15 pre-ECMO variables (including age, sex, birth weight, prior cardiopulmonary arrest, pre-ECMO arterial blood gas results and pre-ECMO ventilator settings) was used to compare outcomes between groups. Survival was not different between the two groups (77%, Group 1: 82%, Group 2, p=0.24), although lung recovery was less frequent in the septic patients (p<.02). Group 1 had a higher incidence of complications as described below:

<u>Complication</u>	<u>Parameter Estimate</u>	<u>Odds Ratio</u>	<u>p-Value</u>
seizures	0.3685	1.446	0.0346
cerebral infarct or hemorrhage	0.8374	2.310	0.0001
dialysis required	0.3909	1.478	0.0131
hypernatremia	0.7369	2.089	0.0019
hyperbilirubinemia	0.8852	2.423	0.0001
dobutamine use	0.6513	1.918	0.0001

Septic neonates are more likely to sustain neurologic, renal, and metabolic complications from ECMO but may still achieve a survival benefit equivalent to those without sepsis. From these data, ECMO should not be withheld from neonates solely on the basis of sepsis.

### 10:20 a.m. INTERMISSION

\*By invitation

### 11:05 a.m. SIMULTANEOUS SCIENTIFIC SESSION F -CONGENITAL HEART DISEASE

**West Ballroom**

**Moderators: Richard A. Jonas, M.D.**

**Julie A. Swain, M.D.**

### 57. QUANTITATIVE EEC - AN INTRAOPERATIVE METHOD TO ASSESS CEREBRAL INJURY FOLLOWING HYPOTHERMIC CIRCULATORY ARREST



Craig K. Mezrow, M.S.\*, Peter S. Midulla, M.D.\*, Ali M. Sadeghi, M.D.\*, Alejandro Gandsas, M.D.\*, Weijia Wang, M.D.\*, Howard H. Shiang, D.V.M.\*, Rosario Zappulla, M.D, Ph.D.\* and Randall B. Griep, M.D.

*New York, New York*

Hypothermic circulatory arrest (HCA) and its alternative, low flow cardiopulmonary bypass (LFCPB), are routinely employed for surgical correction of congenital cardiac anomalies. As the complexity of the repairs has increased, longer durations of HCA have more often been required, heightening concern about cerebral safety. An intraoperative assessment which can reliably predict cerebral injury is essential in order to devise strategies to increase cerebral protection during these procedures. This study shows an excellent correlation between changes in quantitative EEG (QEEG) two hours after HCA and PFCPB and neurological and behavioral evidence of cerebral injury.

Following epidural placement of 4 recording EEG electrodes and baseline neurologic/behavioral assessment, 32 puppies (3 months) were randomly assigned to one of 4 groups after cardiopulmonary bypass cooling to 18C: (1) controls (in which animals were cooled and immediately rewarmed), (2) 30 min HCA, (3) 90 min HCA, (4) 90 min LFCPB. EEG was recorded at baseline (37C), and at 2, 4 and 8 hrs following HCA or LFCPB. Postoperative neurologic and behavioral outcome was assessed 24 hrs after CPB using a scale in which zero is normal and 13 indicates severe neurological injury (coma or death).

Thirty animals survived the experimental protocol: two animals who underwent 90 min of circulatory arrest died, one with possible neurological injury, and one secondary to multiorgan failure. The surviving animals following 90 min HCA had severe neurologic/behavioral deficits. No deficits were observed in the control and 30 min HCA groups, and only one animal following 90 min LFCPB had a slight neurological/behavioral deficit.

QEEG analysis revealed maximal differences between the experimental groups 2 hrs after the start of rewarming. The 90 min HCA group was significantly different from all other groups at this timepoint ( $p < 0.01$ ). Furthermore, 30 min HCA was significantly different from control and LFCPB, despite the absence of neurological/behavioral deficits. No significant differences in QEEG were observed between control and 90 min LFCPB groups. The figure below depicts the relationship between EEG power and neurologic/behavioral score: it allows us to predict with great certainty ( $p < 0.00001$ ) that if EEG power 2 hrs after rewarming is less than 500 uvolts<sup>2</sup>, overt neurologic injury will result. The significant differences between controls and 30 min HCA groups also suggests that QEEG may detect subtle cerebral injury that is not apparent from neurologic/behavioral examination.

This study shows differences in QEEG values 2 hrs after differing durations of HCA at 18C. The data confirm the presence of unequivocal cerebral injury after 90 min HCA, and suggest that after even 30 min HCA, there may be subtle cerebral injury undetected by neurological/behavioral evaluation, although this interval is clinically accepted as safe. In contrast, no QEEG evidence of cerebral dysfunction was apparent after 90 min LFCPB at 18C. This study suggests that QEEG is a sensitive indicator of cerebral injury, and may prove extremely valuable in future studies of strategies for cerebral protection during cardiac surgery.

\*By invitation

## 58. MODIFIED ULTRAFILTRATION IMPROVES CEREBRAL METABOLIC RECOVERY AFTER CIRCULATORY ARREST

Lynne A. Skaryak, M.D.\*, Paul M. Kirshbom, M.D.\*, Louis R. DiBernardo, M.D.\*, Frank H. Kern, M.D.\*, William J. Greeley, M.D.\*, Ross M. Ungerleider, M.D.\* and J. William Gaynor, M.D.\*

*Durham, North Carolina*

*Sponsored by: David C. Sabiston, Jr., M.D., Durham, North Carolina*

Modified ultrafiltration (MUF) utilizes hemofiltration of the bypass circuit and patient after separation from cardiopulmonary bypass (CPB) to reverse hemodilution and edema that occurs during cardiac surgery. MUF has been shown to increase cardiac index and mean arterial pressure and to decrease pulmonary vascular resistance after CPB. This study investigates the effect of MUF on cerebral metabolic recovery following deep hypothermic circulatory arrest (DHCA). Twenty-six piglets (2-3kg) were placed on CPB (37°C) at 100 ml/kg/min and were then cooled to 18°C. All animals underwent 90 min. of DHCA followed by rewarming to 37°C. Global cerebral blood flow (CBF) was measured using Xenon<sup>133</sup> clearance methods. Cerebral metabolic rate of oxygen consumption (CMRO<sub>2</sub>) and cerebral oxygen delivery (cD·O<sub>2</sub>) were calculated. After weaning from CPB animals were divided into groups as follows: CTL (n=10) - observed for 20 min. without any intervention; MUF (n=9) underwent 20 min. of MUF; Tx (n=7)-received transfusion of hemoconcentrated blood over 20 min. CMRC>2, cD·O<sub>2</sub> and HCT were measured: I-pre-CPB, II-immediately post-CPB and III-20 min. post-CPB.

	HCT (% ± S.E.)			CD·O <sub>2</sub> (ml/min ± S.E.)			CMRO <sub>2</sub> (ml/100 gm/min ± S.E.)		
	I	II	III	I	II	III	I	II	III
CTL	27±10	28±09	28±1.5	3.81±0.16	3.50±0.24	277±019‡	2.47±007	2.62±025	1.95±0.15‡
MUF	28±1.7	27±1.2	44±18†‡	3.85±0.16	3.34±0.13	4.98±0.32†‡	2.48±013	2.38±008	3.12±0.24§‡
Tx	30±0.7	28±0.9	42±18†‡	3.89±0.06	3.47±0.35	4.59±0.17†‡	239±015	197±0.29	1.72±0.10

† p<0.05 vs. III-CTL ‡ p<0.05 vs. I & II § p<0.05 vs. III-CTL, Tx ~ p<0.05 vs. I-Tx

These data demonstrate: (1) 90 minutes of DHCA (CTL group) results in impaired CMRO<sub>2</sub> 20 minutes after cessation of CPB. This appears to be from low cD·O<sub>2</sub>. (2) However, simply increasing cD·O<sub>2</sub> by raising the hematocrit does not result in improved CMRO<sub>2</sub> and cerebral metabolism remains impaired following DHCA. (3) Following MUF, cD·O<sub>2</sub> and CMRO<sub>2</sub> increase and indicates that the brain can recover from metabolic dysfunction after DHCA. This ability to acutely improve cerebral metabolism after DHCA has never before been demonstrated. Therefore, it may be possible to reduce brain injury associated with DHCA by using MUF to improve cerebral oxygen utilization after the patient has been weaned from CPB.

\*By invitation

## 59. ENDOTHELIN-1 MEDIATED CORONARY CONSTRICTION IN NEONATAL CARDIOPULMONARY BYPASS: REVERSAL BY NITROGLYCERIN

Francis X. McGowan, Jr., M.D.\*, Peter J. Davis, M.D.\*, Ralph D. Siewers, M.D., Pedro J. del Nido, M.D.\*

*Pittsburgh, Pennsylvania*

Endothelin-1 (ET-1) is an exceedingly potent endogenous vasoconstrictor whose concentrations are increased in sepsis, congestive heart failure, hypoxia and vascular trauma. To determine the role of ET-1 in cardiopulmonary bypass (CPB), we measured plasma ET-1 concentrations in neonates before and after CPB for arterial switch procedures and then studied the effects of clinically relevant ET-1 concentrations upon coronary tone and contractility in normal and reperfused neonatal pig hearts.

ET-1 was measured using a commercially available radioimmunoassay (Amersham). Pulmonary venous blood samples were obtained immediately prior to initiating CPB and 1 hour after separation from CPB in 14 consecutive neonates undergoing arterial switch for transposition of the great arteries (TGA). For comparison, ET-1 was measured in 6 children pre- and post-CPB undergoing repair of atrial septal defects (ASD), umbilical venous blood (N=8), and venous samples from healthy adults (N=14). ET-1 concentrations increased in TGA patients from  $22.9 \pm 0.9$  to  $28.6 \pm 1.0$  pg/ml ( $P < 0.01$ ) and from  $13.2 \pm 0.6$  to  $15.4 \pm 0.6$  pg/ml in ASD patients ( $P < 0.05$ ) after CPB. ET-1 concentrations in pre-CPB TGA infants and neonatal cord blood ( $18.7 \pm 1.0$  pg/ml) were significantly higher ( $P < 0.01$ ) than those in adults ( $10.7 \pm 0.5$  pg/ml) or ASD children.

The myocardial effects of ET-1 were assessed in piglet hearts (aged 4-7 days) using a blood-perfused Langendorff preparation with controlled coronary flow. Coronary perfusion pressure (CPP), peak developed left ventricular pressure (PDP), and oxidative metabolism were measured. Responses in non-ischemic and ischemic-reperfused hearts to ET-1 (20 pg/ml) or ET-1 plus nitroglycerin (NTG; 2 nmol/ml) were quantified (N=8 each group). In another group (N=8 each), the effects of norepinephrine (NE, 1 ng/ml), alone or in combination with ET-1 and NTG, were studied to further evaluate endothelial and smooth muscle function. Data are presented as mean  $\pm$  standard error.

The effects of ET-1 (20 pg/ml) upon CPP (in mm Hg) in normal and reperfused neonatal pig hearts are shown in the Table. NE produced coronary vasodilation pre-ischemia ( $-11 \pm 2\%$ ) that was converted to constriction by ET-1; during reperfusion, ET-1+NE caused significantly greater increases in CPP as compared to non-ischemic hearts ( $55 \pm 4\%$  vs  $26 \pm 2\%$ ,  $P < 0.01$ ) that was also reversed by NTG. ET-1 also reduced PDP ( $-18 \pm 4\%$ ) during reperfusion.

	<u>Baseline</u>	<u>ET-1</u>	<u>ET-1 + NTG</u>
Non-ischemic	$56 \pm 2$	$59 \pm 2$	$48 \pm 3$
Reperfused	$53 \pm 3$	$80 \pm 4^*$	$57 \pm 3^+$

\*  $P < 0.01$  vs Non-ischemic

+  $P < 0.001$  vs ET-1 alone

We conclude that ET-1 concentrations are significantly elevated in neonates and after CPB. When endothelial injury is present (e.g. post-CPB), vasoconstriction caused by clinically relevant concentrations of ET-1 and ET-1 + NE is markedly enhanced. NTG reverses the coronary vasoconstrictor effects of ET-1 before and after ischemia-reperfusion and therefore may be beneficial in the postoperative management of neonates after open heart surgery.

**12:00 p.m. ADJOURN**

\*By invitation

## GEOGRAPHICAL ROSTER

### NECROLOGY

Ronald M. Abel, M.D. Newark, New Jersey  
Herbert D. Adams, M.D. Chester Depot, Vermont  
David G. Ashbaugh, M.D. Seattle, Washington  
Charles P. Bailey, M.D. Marietta, Georgia  
Jean-Paul Cachera, M.D. Meudon, France  
Herbert A. Carlson, M.D. Long Beach, California  
Arthur J. Cracovaner, M.D. New York, New York  
John M. Dorsey, M.D. No. Palm Beach, Florida  
Dwight E. Harken, M.D. Cambridge, Massachusetts  
Paul F. Hausman, M.D. Delafield, Wisconsin  
Edwin C. James, M.D. Grand Fork, North Dakota  
F. John Lewis, M.D. Santa Barbara, California  
Herbert C. Maier, M.D. Avon, Connecticut  
Richard H. Meade, M.D. Grand Rapids, Michigan  
John W. Strieder, M.D. Chestnut Hill, Massachusetts  
Winfred L. Sugg, M.D. Dallas, Texas  
M. Dawson Tyson, M.D. White River Junction, Vermont  
Sigmund A. Wesolowski, M.D. Lynnfield, Massachusetts  
Mark W. Wolcott, M.D. Salt Lake City, Utah

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Kirklin, John W  
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Pacifico, Albert D

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Miller, Joseph I  
Rivkin, Laurence M  
Symbas, Panagiotis  
Williams, Willis H

### **Augusta**

Ellison, Robert G  
Rubin, Joseph W

### **Chickamauga**

Hall, David P

### **Macon**

Dalton, Martin L, Jr  
Sealy, Will C  
Van De Water, Joseph M

### **Savannah**

Yeh, Thomas J

## **HAWAII**

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### **Honolulu**

Ching, Nathaniel P  
Gebauer, Paul W  
McNamara, J Judson

## **IDAHO**

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### **Boise**

Herr, Rodney H

### **Park Ridge**

Baffes, Thomas G  
Levett, James M  
Weinberg, Milton, Jr

### **Peoria**

DeBord, Robert A

### **Springfield**

Wellons, Harry A, Jr

### **Winnetka**

Mackler, S Allen

## **INDIANA**

### **Indianapolis**

Brown, John W  
King, Harold  
King, Robert D  
Mandelbaum, Isidore  
Siderys, Harry

## **IOWA**

### **Cedar Rapids**

Lawrence, Montague S

### **Council Bluffs**

Sellers, Robert D

### **Des Moines**

Dorner, Ralph A  
Phillips, Steven J  
Zeff, Robert H

### **Iowa City**

Behrendt, Douglas M  
Ehrenhaft, Johann L  
Rossi, Nicholas P  
Stanford, William

## **KANSAS**

### **Cunningham**

Allbritten, Frank F, Jr

### **Lawrence**

Miller, Don R

### **Overland Park**

Ashcraft, Keith W  
Holder, Thomas M  
Shawnee Mission  
Adelman, Arthur

### **Wichita**

Sullivan, Henry J  
**Oak Brook**  
Hudson, Theodore R  
Ilbawi, Michel N  
Javid, Hushang  
Jensik, Robert J  
Nigro, Salvatore L

**KENTUCKY**

**Lexington**

Crutcher, Richard R  
Dillon, Marcus L, Jr  
Todd, Edward P J

**Louisville**

Gray, Laman A, Jr  
Mahaffey, Daniel E  
Ransdell, Herbert, Jr

**LOUISIANA**

**Alexandria**

Knoepp, Louis F

**Baton Rouge**

Berry, B Eugene  
Beskin, Charles A

**Metairie**

Ochsner, Alton, Jr

**New Orleans**

Blalock, John B  
DeCamp, Paul T  
Hewitt, Robert L  
Lindsey, Edward S  
McFadden, P Michael  
Mills, Noel L  
Moulder, Peter V  
Ochsner, John L  
O'Neill, Martin J, Jr  
Pearce, Charles W  
Rosenberg, Dennis M  
Schramel, Robert J  
Webb, Watts R

**MAINE**

**Liberty**

Hurwitz, Alfred

**Portland**

Bredenber, Carl E  
Drake, Emerson H

**Rockport**

Swenson, Orvar

**Windham**

Hiebert, Clement

**MARYLAND**

**Baltimore**

Attar, Safuh  
Baker, R Robinson  
Baumgartner, William A  
Blair, Emil  
Dodrill, Forest D  
Gardner, Timothy J

Shemin, Richard J  
Starkey, George W B  
Thurer, Robert L  
Vlahakes, Gus J  
Weintraub, Ronald

**Boylston**

Okike, Okike N

**Brookline**

Madoff, Irving M

Tocker, Alfred M

Gott, Vincent L  
Haller, J Alex, Jr  
McLaughlin, Joseph S  
Michelson, Elliott  
Salomon, Neal W  
Turney, Stephen Z  
Watkins, Levi, Jr

**Bethesda**

Pass, Harvey I

**Chevy Chase**

Iovine, Vincent M

**Ellicott City**

MacManus, Joseph E

**Towson**

Brawley, Robert K.

**Worton**

Walkup, Harry E

**MASSACHUSETTS**

**Boston**

Akins, Gary W  
Austen, W Gerald  
Barsamian, Ernest M  
Berger, Robert L  
Bougas, James A  
Buckley, Mortimer J  
Burke, John F  
Castaneda, Aldo R  
Cleveland, Richard J  
Cohn, Lawrence H  
Collins, John J  
Daggett, Willard M  
Daly, Benedict D T  
Ellis, F Henry, Jr  
Frank, Howard A  
Gaensler, Edward A  
Grillo, Hermes C  
Hilgenberg, Alan D  
Johnson, Robert G  
Jonas, Richard A  
Lazar, Harold L  
Levitsky, Sidney  
LoCicero, Joseph  
Mathisen, Douglas J  
Mayer, John E  
Moncure, Ashby C  
Neptune, Wilford B  
Rheinlander, Harold F  
Russell, Paul S  
Scannell, J Gordon

**MICHIGAN**

**Ann Arbor**

Bartlett, Robert H  
Bolling, Steven F  
Bove, Edward L  
Deeb, G Michael  
Gago, Otto  
Greenfield, Lazar J  
Kirsh, Marvin M



**Burlington**  
Shahian, David M  
**Cambridge**  
Malcolm, John A  
**Chestnut Hill**  
Laforet, Eugene G  
**Concord**  
Soutter, Lamar  
**Dover**  
Black, Harrison  
**Framingham**  
Schuster, Samuel R  
**Medford**  
Desforges, Gerard  
**Methuen**  
Wilson, Norman J  
**North Andover**  
Cook, William A  
**Shrewsbury**  
Moran, John M  
**Springfield**  
Engelman, Richard M  
Rousou, John A  
**Vineyard Haven**  
Malm, James R  
**West Roxbury**  
Bernhard, William F  
Khuri, Shukri F  
**Westport Harbor**  
Findlay, Charles W, Jr  
**Williamstown**  
Wilkins, Earle W, Jr  
**Worcester**  
Vander Salm, Thomas J

**Rochester**  
Bernatz, Philip E  
Danielson, Gordon K  
McGoan, Dwight C  
McGregor, Christopher G A  
Olsen, Arthur M  
Orszulak, Thomas A  
Pairolero, Peter C  
Payne, W Spencer  
Puga, Francisco J  
Schaff, Hartzell V  
Trastek, Victor F  
**St Paul**  
Lillehei, C Walton  
Miller, Fletcher A  
**Shoreview**  
Deac, Radu C.  
**Waubun**  
DeNiord, Richard N  
**MISSISSIPPI**  
**Carthage**  
Logan, William D, Jr  
**Jackson**  
Hardy, James D  
Johnston, J Harvey, Jr  
Netterville, Rush E  
**MISSOURI**  
**Bridgeton**  
Codd, John E

Morris, Joe D  
Neerken, A John  
Orringer, Mark B  
Prager, Richard L  
Sloan, Herbert  
**Bloomfield Township**  
Timmis, Hilary H  
**Detroit**  
Arbulu, Agustin  
Silverman, Norman A  
Steiger, Zwi  
Stephenson, Larry W  
Wilson, Robert F  
**Grand Rapids**  
Harrison, Robert W  
Rasmussen, Richard A  
Tomatis, Luis A  
**Grosse Pointe**  
Benson, Clifford D  
**West Bloomfield**  
Arciniegas, Eduardo  
**MINNESOTA**  
**Coon Rapids**  
Gannon, Paul G  
Mendota Heights  
Dennis, Clarence  
**Minneapolis**  
Arom, Kit V  
Bolman, R Morton, III  
Emery, Robert W  
Foker, John E  
Garamella, Joseph J  
Helseth, Hovald K  
Humphrey, Edward W  
Kaye, Michael P  
Riser, Joseph C  
Molina, J Ernesto  
Nicoloff, Demetre M

**St Louis**  
Earner, Hendrick B  
Baue, Arthur E  
Connors, John P  
Cooper, Joel D  
Cox, James L  
Ferguson, Thomas B  
Flye, M Wayne  
Johnson, Frank E  
Kaiser, George C  
Kouchoukos, Nicholas T  
Lewis, J Eugene, Jr  
McBride, Lawrence R  
Naunheim, Keith S  
Pasque, Michael K  
Patterson, G Alec  
Pennington, D Glenn  
Roper, Charles L  
Spray, Thomas L  
Weldon, Clarence S  
Willman, Vallee L  
**MONTANA**  
**Missoula**  
Oury, James H  
**Twin Bridges**  
Lower, Richard R  
**NEBRASKA**  
**Omaha**  
Fleming, William H

**Chesterfield**

Bergmann, Martin

**Columbia**

Bryant, Lester R  
Curtis, Jack J  
Silver, Donald  
Walls, Joseph T

**Kansas City**

Benoit, Hector W, Jr  
Borkon, A Michael  
Killen, Duncan A  
Mayer, John H, Jr  
Padula, Richard T  
Piehler, Jeffrey M  
Reed, William A  
Van Way, Charles W, III

**Mount Vernon**

Campbell, Daniel C, Jr

**Camden**

Camishion, Rudolph C  
DelRossi, Anthony J

**East Orange**

Auerbach, Oscar

**Hackensack**

Hutchinson, John E, III

**Jersey City**

Demos, Nicholas J

**Millburn**

Personnel, Victor

**Moorestown**

Morse, Dryden P

**Morristown**

Parr, Grant V S

**Neptune**

Roberts, Arthur J

**New Brunswick**

Lewis, Ralph J  
MacKenzie, James W  
Scholz, Peter M

**Newark**

Donahoo, James  
Gielchinsky, Isaac  
Swan, Kenneth G

**Paterson**

Bregman, David

**Tenafly**

Gerst, Paul H

**NEW MEXICO****Albuquerque**

Edwards, W Sterling

**Las Vegas**

Thai, Alan P

**Santa Fe**

Davila, Julio C

**Silver City**

Waddell, William R

**NEW YORK****Albany**

Foster, Eric D

**Bay Shore**

Ryan, Bernard J

**Bronx**

Altai, Lari A  
Brodman, Richard F  
Fell, Stanley C

Schultz, Richard D

**NEVADA****Las Vegas**

Little, Alex G  
Swain, Julie A

**NEW HAMPSHIRE****Franconia**

Taylor, Warren J

**Jaffrey**

Woods, Francis M

**NEW JERSEY****Alpine**

Holswade, George R

**Bellville**

Gerard, Franklyn P

**Browns Mills**

Fernandez, Javier  
McGrath, Lynn B

Ford, Joseph M

Prater, Robert W M

Gay, William A, Jr

Hirose, Teruo

**Brooklyn**

Cunningham, Joseph N, Jr

Levowitz, Bernard S

Sawyer, Philip N

**Buffalo**

Adler, Richard H

Andersen, Murray N

Bhayana, Joginder N

Hoover, Eddie L

Lajos, Thomas Z

**Cooperstown**

Blumenstock, David A

**Fayetteville**

Bugden, Walter F

Effler, Donald B

**Floral Park**

Crastnopol, Philip

**Flushing**

Strevey, Tracy E, Jr

**Lido Beach**

Hines, George L

**Loudonville**

Alley, Ralph D

**New Hyde Park**

Amato, Joseph J

**New Rochelle**

Rubin, Morris

**New York**

Acinapura, Anthony J

Adams, Peter X

Anagnostopoulos, C E

Bains, Manjit S

Seattle, Edward, Jr

Bloomberg, Allan E

Boyd, Arthur D

Burt, Michael E

Cahan, William G

Clauss, Roy H

Conklin, Edward F

Culliford, Alfred T

Ergin, M Arisan

Friedlander, Ralph

Galloway, Aubrey C, Jr

Ginsberg, Robert J  
Gold, Jeffrey P  
Green, George E  
Griep, Randall B  
Holman, Cranston W  
Isom, O Wayne  
Jaretzki, Alfred, III  
King, Thomas C  
Kirschner, Paul A  
Krieger, Karl H  
Lambert, Adrian  
Litwak, Robert S  
Martini, Nael  
McCord, Colin W  
McCormack, Patricia M  
Nealon, Thomas F, Jr  
Quaegebeur, Jan M  
Redo, S Frank  
Reemtsma, Keith  
Rose, Eric A  
Rusch, Valerie W  
Skinner, David B  
Smith, Craig R  
Spencer, Frank C  
Spotnitz, Henry M  
Steichen, Felicien M  
Subramanian, Valavanur A  
Tice, David A  
Tyras, Denis H  
Veith, Frank J  
Wichern, Walter, Jr  
Wolff, William I

**Patchogue**  
Finnerty, James

**Plattsburg**  
Potter, Robert T

**Rochester**  
Graver, William L  
DeWeese, James A  
Hicks, George L  
Schwartz, Seymour I  
Stewart, Scott

**Roslyn**  
Thomson, Norman B, Jr  
Wisoff, B George

**Saranac Lake**  
Decker, Alfred M, Jr

**Winston-Salem**  
Cordell, A Robert  
Crosby, Ivan K  
Hammon, John W, Jr  
Hudspeth, Allen S  
Meredith, Jesse H  
Mills, Stephen A

**OHIO**

**Chagrin Falls**  
Cross, Frederick S

**Cincinnati**  
Albers, John E  
Callard, George M  
Flege, John B, Jr  
Gonzalez, Luis L  
Helmsworth, James A  
Hiratzka, Loren F  
Ivey, Tom D  
Wilson, James M  
Wright, Creighton B

**Scarsdale**  
Robinson, George

**Scottsville**  
Emerson, George L

**Slingerlands**  
Kausel, Harvey W

**Staten Island**  
Garzon, Antonio A

**Stony Brook**  
Soroff, Harry S

**Syracuse**  
Brandt, Berkeley, III  
Meyer, John A  
Parker, Frederick, Jr

**Valhalla**  
Moggio, Richard A  
Reed, George E

**NORTH CAROLINA**

**Asheville**  
Belts, Reeve H  
Kroncke, George M  
Scott, Stewart M  
Takaro, Timothy

**Chapel Hill**  
Bowman, Frederick, Jr  
Keagy, Blair A  
Starek, Peter J K  
Wilcox, Benson R

**Charlotte**  
Robicsek, Francis  
Selle, Jay G  
Taylor, Frederick H

**Durham**  
Jones, Robert H  
Lowe, James E  
Oldham, H N, Jr  
Sabiston, David C  
Wolfe, Walter G  
Young, W Glenn, Jr

**Greenville**  
Chitwood, W Randolph

**Oriental**  
Deaton, W Ralph, Jr

**Pinchurst**  
Fischer, Walter W

**Sugar Grove**  
Gentsch, Thomas O

**Oklahoma City**  
Elkins, Ronald C  
Felton, Warren L, II  
Fisher, R Darryl  
Greer, Allen E  
Munnell, Edward R  
Williams, G Rainey  
Zuhdi, M Nazih

**OREGON**

**Days Creek**  
Miller, Arthur C

**Portland**  
Cobanoglu, Adnan  
Krause, Albert H  
Lemmer, John H, Jr  
Okies, J Edward  
Poppe, J Karl  
Starr, Albert

**PENNSYLVANIA**

**Abington**

Yee, Edward S

**Cleveland**

Ankeney, Jay L  
Cosgrove, Delos M  
Geha, Alexander S  
Groves, Laurence K  
Kay, Earle B  
Loop, Floyd D  
Lytle, Bruce W  
Rice, Thomas W  
Snow, Norman J  
Van Heeckeren, Daniel W

**Columbus**

Clatworthy, H W, Jr  
Davis, J Terrance  
Kakos, Gerard S  
Oman, James W  
Meckstroth, Charles  
Myerowitz, P David  
Williams, Thomas E, Jr

**Dayton**

DeWall, Richard A

**Pepper Pike**

Mendelsohn, Harvey J

**OKLAHOMA**

**Jenks**

LeBeck, Martin B

**Lawton**

Barnhorst, Donald A

**Philadelphia**

Addonizio, Paul V  
Bowles, L Thompson  
Brockman, Stanley K  
Diehl, James T  
DiSesa, Verdi J  
Edie, Richard N  
Edmunds, L Henry, Jr  
Fineberg, Charles  
Goldberg, Melvyn  
Kaiser, Larry R  
Levine, Frederick H  
MacVaugh, Horace, III  
Nemir, Paul, Jr  
Norwood, William I

**Pittsburgh**

Armitage, John M  
Bahnson, Henry T  
Clark, Richard E  
Ford, William B  
Griffith, Bartley P  
Hardesty, Robert L  
Magovern, George J  
Pontius, Robert G  
Rams, James J  
Siewers, Ralph D

**Rosemont**

Sink, James D  
Templeton, John, III

**Sayre**

Sewell, William H

**Villanova**

Mundth, Eldred D

**Wayne**

Hargrove, W. Clark III  
Lemmon, William M

**Wyncote**

Mendelsohn, Edwin

Frobese, Alfred S

**Bethlehem**

Snyder, John M

**Bristol**

Dunn, Jeffrey M

**Bryn Mawr**

Haupt, George J

**Camp Hill**

Pennock, John L

**Carlisle**

DeMuth, William, Jr

**Darby**

McKeown, John J, Jr

**Erie**

Kerth, William J

**Hershey**

Campbell, David B

Myers, John L

Pae, Walter E, Jr

Pierce, William S

Waldhausen, John A

**Johnstown**

Kolff, Jacob

**Lancaster**

Bonchek, Lawrence I

Rosemond, George P

Witmer, Robert H

**SOUTH CAROLINA**

**Charleston**

Bradham, R Randolph

Crawford, Fred A, Jr

Kratz, John M

Parker, Edward F

Sade, Robert M

**Columbia**

Almond, Carl H

**Isle of Palms**

Mullen, Donald C

**Landrum**

Stayman, Joseph W

**Spartanburg**

Utley, Joe E

**TENNESSEE**

**Knoxville**

Blake, Hu Al

Brott, Walter H

Domm, Sheldon E

**Memphis**

Cole, Francis H

Eastridge, Charles E

Garrett, H Edward

Howard, Hector S, Jr

Hughes, Felix A, Jr

McBurney, Robert P

Pate, James W

Robbins, S Gwin, Sr

Rosensweig, Jacob

Skinner, Edward F

Watson, Donald C

**Nashville**

Alford, William, Jr

Bender, Harvey W, Jr

Gobbel, Walter G, Jr

Merrill, Walter H

Sawyers, John L

**Wynnewood**

Wallace, Herbert W

**Yardley**

Sommer, George N, Jr

**RHODE ISLAND****Providence**

Karlson, Karl E

Moulton, Anthony L

Singh, Arun K

**Burnet**

Ross, Raleigh R

**Coppell**

McPhail, Jasper L

**Dallas**

Adam, Maurice

Estrera, Aaron S

Holland, Robert H

Lambert, Gary J

Mills, Lawrence J

Paulson, Donald L

Platt, Melvin R

Razzuk, Maruf A

Ring, W Steves

Seybold, William D

Urschel, Harold, Jr

**Dilley**

Hood, Richard H, Jr

**El Paso**

Glass, Bertram A

**Galveston**

Conti, Vincent R

Derrick, John R

Tyson, Kenneth R T

Zwischenberger, Joseph B

**Houston**

Beall, Arthur C, Jr

Burdette, Walter J

Cooley, Denton A

DeBakey, Michael E

Frazier, Oscar H

Hall man, Grady L

Henly, Walter S

Jones, James W

Mattox, Kenneth L

Mountain, Clifton F

Ott, David A

Overstreet, John W

Reul, George J, Jr

Roth, Jack A

Walker, William E

Wukasch, Don C

**Kemp**

Davis, Milton V

**Lubbock**

Bricker, Donald L

Feola, Mario

Wallsh, Eugene

**Lynchburg**

Moore, Richmond L

**McLean**

Conrad, Peter W

Mills, Mitchell

**Reston**

Boyd, Thomas F.

Scott, Henry W, Jr

Stoney, William S

Thomas, Clarence, Jr

**Sparta**

Labrosse, Claude C

**TEXAS****Amarillo**

Sutherland, R Duncan

**Austin**

Hood, R Maurice

**San Antonio**

Cohen, David J

Dooley, Byron N

Heaney, John P

Treasure, Robert L

Trinkle, J Kent

**Shepherd**

Morris, George C, Jr

**Temple**

Brindley, G V, Jr

**Woodville**

Harrison, Albert W

**UTAH****Salt Lake City**

Cutler, Preston R

Doty, Donald B

Liddle, Harold V

Mortensen, J D

Nelson, Russell M

**VERMONT****Burlington**

Miller, Donald B

**Richford**

Grondin, Charles M

**West Dover**

Humphreys, G H, II

**VIRGINIA****Altavista**

Pierucci, Louis Jr.

**Annandale**

Akl, Bechara F

Burton, Nelson A

Lefrak, Edward A

**Arlington**

Klepser, Roy G

**Aylett**

Gwathmey, Owen

**Charlottesville**

Dammann, John F

Daniel, Thomas M

Kron, Irving L

Minor, George R

Muller, William, Jr

Nolan, Stanton P

Spotnitz, William D

**Falls Church**

Zajtchuk, Rostik

**WEST VIRGINIA****Charlestown**

Walker, James H

**Huntington**

Gonzalez-Lavin, Lorenzo

**Morgantown**

Graeber, Geoffrey M

**Richmond**

Bosher, Lewis H, Jr  
 Brooks, James W  
 Cole, Dean B  
 Wechsler, Andrew S

**WASHINGTON****Bellingham**

Varco, Richard L

**Friday Harbor**

Lawrence, G Hugh

**Issaquah**

Jarvis, Fred J

**Kirkland**

Mills, Waldo O

**Poulsbo**

Malette, William G

**Seattle**

Anderson, Richard P  
 Dillard, David H  
 Hill, Lucius D, III  
 Jones, Thomas W  
 Li, Wei-I  
 Manhas, Dev R  
 Mansfield, Peter B  
 Miller, Donald W, Jr  
 Rittenhouse, Edward A  
 Sauvage, Lester  
 Thomas, George I  
 Verrier, Edward D

**Spokane**

Berg, Ralph, Jr

Gustafson, Robert A  
 Hill, Ronald C  
 Murray, Gordon F  
 Warden, Herbert E

**Parkersburg**

Tarnay, Thomas J

**WISCONSIN****Eau Claire**

McEnany, M Terry

**Madison**

Chopra, Paramjeet S  
 Mentzer, Robert M, Jr  
 Young, William P

**Marshfield**

Myers, William O  
 Ray, Jefferson F, III  
 Sautter, Richard D

**Mequon**

Narodick, Benjamin

**Milwaukee**

Johnson, W Dudley  
 Litwin, S Bert  
 Olinger, Gordon N  
 Tector, Alfred J

**West Bend**

Gardner, Robert J

**WYOMING****Teton Village**

Kaunitz, Victor H

**CANADA****ALBERTA****Calgary**

Bharadwaj, Baikunth  
 Miller, George E

**Edmonton**

Callaghan, John C  
 Gelfand, Elliot T  
 Sterns, Laurence P

**BRITISH COLUMBIA****Vancouver**

Allen, Peter  
 Ashmore, Phillip G  
 Jamieson, W R Eric  
 Tyers, G Frank O

**Victoria**

Stenstrom, John D

**West Vancouver**

Robertson, Ross

**MANITOBA****Winnipeg**

Barwinsky, Jaroslaw  
 Cohen, Morley

**NOVA SCOTIA****Halifax**

Landymore, Roderick W  
 Murphy, David A

**Mabou**

Thomas, Gordon W

**ONTARIO****Collingwood**

Heimbecker, Raymond

**London**

McKenzie, F Neil  
 Novick, Richard J

**North York****Sudbury**

Field, Paul  
 Walker, George R

**Toronto**

Baird, Ronald J  
 Bigelow, Wilfred G  
 Coles, John G  
 David, Tirone E  
 Delarue, Norman C  
 McKneally, Martin F  
 Mickleborough, Lynda L  
 Pearson, F Griffith  
 Salerno, Tomas A  
 Scully, Hugh E  
 Todd, Thomas R J  
 Trimble, Alan S  
 Trusler, George A  
 Weisel, Richard D  
 Williams, William G

**Westbrook**

Lynn, R Beverley

**QUEBEC****Montreal**

Blundell, Peter E  
 Chartrand, Claude C. C  
 Chiu, Chu-Jeng (Ray)  
 Cossette, Robert  
 Dobell, Anthony R  
 Duranceau, Andre C H  
 Lepage, Gilles  
 MacLean, Lloyd D  
 Morin, Jean E  
 Mulder, David S  
 Pelletier, Conrad L  
 Scott, Henry J

Goldman, Bernard S  
**Nottawa**  
Key, James A  
**Ottawa**  
Keon, Wilbert J

**Sainte-Foy**  
DesLauriers, Jean  
**Sillery**  
Grondin, Pierre

## OTHER COUNTIES

### AFGHANISTAN

**Kabul**  
Hankins, John R

### ARGENTINA

**Buenos Aires**  
Favaloro, Rene G

### AUSTRALIA

### QUEENSLAND

**Brisbane**  
O'Brien, Mark F

### SOUTH AUSTRALIA

**Piccadilly**  
Sutherland, H D'Arcy

### VICTORIA

**Melbourne**  
Nossal, Gustav J V

### AUSTRIA

**Leonding**  
Bruecke, Peter E

**Salzburg**  
Unger, Felix H

**Vienna**  
Wolner, Ernst

### BELGIUM

**Bertem**  
Sergeant, Paul T

### BRAZIL

**Rio de Janeiro**  
Meier, Milton A

**Sao Paulo**  
Jatene, Adib D  
Zerbini, E J

### ENGLAND

**Bath, Avon**  
Belsey, Ronald

**Cambridge**  
Kennedy, John H

**Herefordshire**  
Smith, Roger A

**London**  
Braimbridge, Mark V  
de Leval, Marc R  
Lennox, Stuart C  
Lincoln, Christopher R  
Ross, Donald N

**Naples**  
Cotrufo, Maurizio

**Rome**  
Marcelletti, Carlo

### JAPAN

**Kanazawa**  
Iwa, Takashi

**Kitakyushushi**  
Miyamoto, Alfonso T

**Osaka**  
Kawashima, Yasunaru

**Sendai**  
Mohri, Hitoshi

**Tokyo**

Stark, Jaroslav F  
Taylor, Kenneth M  
Thompson, Vernon C  
Yacoub, Magdi

### FINLAND

**Helsinki**  
Mattila, Severi P

### FRANCE

**Bordeaux**  
Couraud, Louis  
Fontan, Francis M

**Montpellier**  
Thevenet, Andre A

**Paris**  
Binet, Jean-Paul  
Blondeau, Philip  
Cabrol, Christian E A  
Carpentier, Alain F  
Piwnica, Armand H  
Planche, Claude

**Suresnes**  
Bachet, Jean E

### GERMANY

**Aachen**  
Messmer, Bruno J

**Hannover**  
Borst, Hans G

**Munchen**  
Sebening, Fritz

**Neuss**  
Bircks, Wolfgang H

**GUATEMALA**  
**Guatemala City**  
Herrera, Rodolfo

**INDIA**  
**Raiputana**  
Van Allen, Chester M

### IRELAND

**Dublin**  
O'Malley, Eoin

**ITALY**  
**Bergamo**  
Parenzan, Lucio

**Milan**  
Peracchia, Alberto

### SAUDI ARABIA

**Riyadh**  
Duran, Carlos Gomez  
Merendino, K Alvin

### SCOTLAND

**Clydebank**  
Lawrie, Gerald M.

**Edinburgh**  
Logan, Andrew

**Glasgow**  
Wheatley, David J

### SPAIN

**Madrid**  
Rivera, Ramiro

Imai, Yasuharu  
Wada, Juro J  
**MONACO**  
**Monte Carlo**  
Dor, Vincent  
**NEW ZEALAND**  
**Auckland**  
Barratt-Boyes, Sir Brian  
**P.R. OF CHINA**  
**Beijing**  
Ying-Kai, Wu  
**PORTUGAL**  
**Lisbon**  
Macedo, Manuel E M  
**RUSSIA**  
**Moscow**  
Bockeria, Leo A  
Burakovsky, Vladimir I

**SWEDEN**  
**Sollentuna**  
Bjork, Viking O  
**SWITZERLAND**  
**Arzier**  
Hahn, Charles J  
**Fully**  
Naef, Andreas P  
**Zurich**  
Senning, Ake  
Turina, Marko I  
**UNITED ARAB EMIRATES**  
**Abu Dhabi**  
Brom, A Gerard  
**VENEZUELA**  
**Caracas**  
Tricerri, Fernando E

**THE AMERICAN ASSOCIATION FOR  
THORACIC SURGERY  
Charter Members  
June 17, 1917**

E. Wyllis Andrews	Arthur A. Law
John Auer	William Lerche
Edward R. Baldwin	Howard Lienthal
Walter M. Boothby	William H. Luckett
William Branower	Morris Manges
Harlow Brooks	Walton Martin
Lawrason Brown	Rudolph Matas
Kenneth Bulkley	E.S. McSweeney
Alexis Carrel	Samuel J. Metzler
Norman B. Carson	Willy Meyer (Founder)
J. Frank Corbett	James Alexander Miller
Armistead C. Crump	Robert T. Miller
Charles N. Dowd	Fred J. Murphy
Kennon Dunham	Leo S. Peterson
Edmond Melchior Eberts	Eugene H. Pool
Max Einhorn	Walter I. Rathbun
Herman Fischer	Martin Rehling
Albert H. Garvin	B. Merrill Ricketts
Nathan W. Green	Samuel Robinson
John R. Hartwell	Charles I. Scudder
George J. Heuer	William H. Stewart
Chevalier Jackson	Franz Torek
H.H. Janeway	Martin W. Ware
James H. Kenyon	Abraham O. Wilensky
Adrian V. S. Lambert	Sidney Yankauer



**BY-LAWS OF  
THE AMERICAN ASSOCIATION  
FOR THORACIC SURGERY**

**ARTICLE I. NAME**

The name of this Corporation is The American Association for Thoracic Surgery (hereinafter the "Association").

**ARTICLE II. PURPOSE**

The purposes of the Association shall be:

To associate persons interested in, and carry on activities related to, the science and practice of thoracic surgery, the cure of thoracic disease and the related sciences.

To encourage and stimulate investigation and study that will increase the knowledge of intrathoracic physiology, pathology and therapy, and to correlate and disseminate such knowledge.

To hold scientific meetings featuring free discussion of problems and developments relating to thoracic surgery, and to sponsor a journal for the publication of scientific papers presented at such meetings and other suitable articles.

To succeed to, and continue to carry on the activities formerly conducted by The American Association for Thoracic Surgery, an unincorporated association.

**ARTICLE III. MEMBERSHIP**

Section 1. There shall be three classes of members: Honorary, Senior, and Active. Admission to membership in the Association shall be by election. Membership shall be limited, the limits on the respective classes to be determined by these By-Laws. Only Active and Senior Members shall have the privilege of voting or holding office, except as provided by these By-Laws. Honorary members shall have the privilege of voting but shall not be eligible to hold office.

Section 2. Honorary Membership shall be reserved for such distinguished persons as may be deemed worthy of this honor by the Council with concurrence of the Association.

Section 3. The number of Senior Members shall be unlimited. Active Members automatically advance to Senior Membership at the age of sixty-five years. In addition, a younger Active Member may be eligible for Senior Membership if incapacitated by disability, but for no other reason.

Section 4. Active Membership shall be limited to six hundred. A candidate to be eligible must be a citizen of the United States of America or Canada, unless in unusual cases this citizenship requirement shall have been waived by the Council. The candidate shall have achieved distinction in the thoracic field or shall have made a meritorious contribution to knowledge pertaining to thoracic disease or its surgical treatment.

Section 5. Election to Honorary, Senior or Active Membership shall be for life, subject to the provisions of Section 8 following. All new members shall be elected directly to Honorary or Active status.

Section 6. Candidates for membership in this Association must be formally nominated and seconded, in an approved manner, by not less than three Active, Senior or Honorary Members. Such nomination must have been in the hands of the Membership Committee for not less than four months, and the name of the candidate must have been distributed to all members of the Association before final action may be taken on any new candidate for election to Active Membership. Provided the foregoing requirements have been met and the candidates have been approved by the Membership Committee and by the Council, their names shall be presented to the Association at a regularly convened annual meeting for final action. A three-fourths vote of those present and voting shall be required to elect. Any candidate for membership in the Association who has failed of election three times shall automatically cease to be a candidate and may not be renominated until after a lapse of three years.

Section 7. The report of the Membership Committee shall be rendered at the second executive session of each annual meeting of the Association. Candidates shall be presented in groups in the following order:

Candidates for Honorary Membership; retirement of Active Members to Senior Membership; Candidates for Active Membership; members dropped from the rolls of the Association.

Section 8. Membership may be voluntarily terminated at any time by members in good standing. The council, acting as Board of Censors, may recommend the expulsion of a member on the grounds of moral or professional delinquency, and submit his name, together with the grounds of complaint, to the Association as a whole at any of the regularly convened meetings, after giving such member ample opportunity to appear in his own behalf.

Section 9. The Council shall recommend that any Active Member whose dues are in arrears for two years, or who has been absent, without sufficient excuse, from three consecutive annual meetings, shall have his membership terminated.

Section 10. Notwithstanding Section 9, any member of the Association over 65 years of age is excused from the attendance requirement and upon his specific request may likewise be excused from the payment of dues.

#### **ARTICLE IV. Board of Directors ("Council")**

Section 1. The Board of Directors of the Association shall be called the Council and shall be composed of the President, Vice-President, Secretary, Treasurer, five Councilors and the Editor of the Association shall be a member *ex-officio* without vote. All members of the Council must be Active or Senior Members of the Association, except that the Editor may be an Honorary Member.

Section 2. The Council shall be the governing body of the Association, and shall have full power to manage and act on all affairs of the Association, except as follows:

- a. It may not alter the initiation fees or annual dues, or levy any general assessments against the membership, except that it may, in individual cases, waive annual dues or assessments.
- b. It may not change the Articles of Incorporation or By-Laws.
- c. It may neither elect new members nor alter the status of existing members, other than to apply the provisions of Article III, Section 8.
- d. It may not deplete the principal of the Endowment Fund.

Section 3. At the conclusion of the annual meeting, the retiring President shall automatically become a Councilor for a one-year term of office. One of the other four Councilors shall be elected at each annual meeting of the Association to serve for a four-year term of office in the place of the elected Councilor whose term expires at such meeting, but no Councilor may be re-elected to succeed himself. Any Councilor so elected shall take office upon the conclusion of the annual meeting at which he is elected.

Section 4. Vacancies in the office of Councilor shall be temporarily filled by the Council subject to approval of the Association at the next annual meeting of the Association.

#### **ARTICLE V. Officers**

Section 1. The officers of the Association shall be President, a Vice-President, a Secretary, and a Treasurer. All officers must be Active or Senior Members of the Association. Said officers shall be *ex officio* members of the Council of the Association.

Section 2. The Council may, for the purposes of Article IV, give status as officers of the Association to the individual members of an *ad hoc* Committee appointed by the Council.

Section 3. The President, Vice-President, Secretary and Treasurer shall be elected at the annual meeting of the Association and shall take office upon conclusion of the meeting. The President and the Vice-President shall be elected for a one-year term of office and neither may be re-elected to succeed himself in the same office, unless such officer is filling the unexpired term of an officer previously elected to such office. The Secretary and the Treasurer shall be elected for a one-year term of office and may be re-elected for not more than four additional terms.

Section 4. The President of the Association shall perform all duties customarily pertaining to the office of President. He shall preside at all meetings of the Association and at all meetings of the Council.

Section 5. The Vice-President of the Association shall perform all duties customarily pertaining to the office of the Vice-President, both as to the Association and the Council. In the event of a vacancy occurring in the office of President, the Council shall advance the Vice-President to the Presidency and appoint an interim Vice-President.

Section 6. The Secretary of the Association shall perform all duties customarily pertaining to the office of Secretary. He shall serve as Secretary of the Association and as Secretary of the Council. When deemed appropriate an Active or Senior Member may be elected to serve as an understudy to the Secretary in anticipation of the letter's retirement from office.

Section 7. The Treasurer of the Association shall perform all duties customarily pertaining to the office of Treasurer. He shall serve as Treasurer of the Association and shall also serve as custodian of the Endowment Fund.

Section 8. The Editor of the Association is not an officer of the Association. He shall be appointed by the Council at its annual meeting; provided, however, that such appointment shall not become effective until approved by the Association at the annual meeting of the Association. The Editor shall be appointed for a five-year term and may not be appointed to more than two successive terms; provided, however, that an Editor completing two years or less of the unexpired term of a previous Editor may be appointed for two successive five-year terms. The Editor shall serve as the Editor of the Official Journal and shall be *ex officio* the Chairman of the Editorial Board and a member of the Council of the Association without vote.

Section 9. Vacancies occurring among the officers named in Section 1 or a vacancy in the position of Editor shall be temporarily filled by the Council, subject to approval of the Association at the next meeting of the Association.

#### **ARTICLE VI. Committees**

Section 1. The Council is empowered to appoint a Membership Committee, a Program Committee, a Necrology Committee and such other committees as may in its opinion be necessary or desirable. All such committees shall render their reports at an executive session of the Association, except that no *ad hoc* committee need report unless so directed by the Council.

Section 2. The Membership Committee shall consist of seven Active or Senior Members. The Council may appoint not more than one of its own members to serve on this Committee. The duties of the Membership Committee are to investigate all candidates for membership in the Association and to report its findings as expeditiously as possible to the Council through the Secretary of the Association. This Committee is also charged with searching the literature of this and other countries to the end that proper candidates may be presented to the Association for consideration. Appointment to this Committee shall be for a period of one year, and not more than five of the members may be reappointed to succeed themselves. This Committee is also charged with maintaining a record of membership attendance and participation in the scientific programs and reporting to the affected members and to the Council any deviations from the requirement of Article VIII, Section 4, of these By-Laws.

Section 3. The Program Committee shall consist of at least six members: the President, the Vice President, the Secretary and at least six members-at-large, two representing each of the areas of adult cardiac, pediatric cardiac and general thoracic surgery. Three of these members-at-large shall be appointed each year by the President for a two-year term. Additional committee members shall be appointed for one-year terms. The Editor shall serve as an ex-officio member of the Committee without vote. The duties of this Committee shall be to arrange, in conformity with instructions from the Council, the scientific program for the annual meeting.

Section 4. The Necrology Committee shall consist of one or more Active or Senior Members. Appointments to this Committee shall be for a one-year term of office. Any or all members of this Committee may be reappointed to succeed themselves. The Council may, if it so desires, appoint one of its own members to serve as Chairman of this Committee. The duties of the Necrology Committee shall be to prepare suitable resolutions and memorials upon all deaths of members of the Association and to report such deaths at every annual meeting.

Section 5. The Nominating Committee shall consist of the five (5) immediate Past Presidents of the Association. The most senior Past President shall serve as Chairman. This Committee shall prepare a slate of nominees for Officers and Councilors upon instruction from the Council as to the vacancies which are to be filled by election and shall present its report at the Second Executive Session of the Annual Meeting.

Section 6. The Association as a whole may authorize the Council to appoint Scientific or Research Committees for the purpose of investigating thoracic problems and may further authorize the Council to support financially such committees to a limited degree. When Scientific or Research Committees are authorized by the Association, the Council shall appoint the Chairmen of these Committees, with power to organize their committees in any way best calculated to accomplish the desired object, subject only to the approval of the Council. Financial aid rendered to such Committees shall not exceed such annual or special appropriations as may be specifically voted for such purposes by the Association as a whole. Members are urged to cooperate with all Scientific or Research Committees of the Association.

Section 7. The Evarts A. Graham Memorial Traveling Fellowship Committee shall consist of seven members: the President, Secretary, and Treasurer of the Association and four members-at-large, one member being appointed by the President each year to serve a term of four year. The Chairman shall be the member-at-large serving his fourth year. The duties of the Committee shall be to recommend Fellowship candidates to the Graham Education and Research Foundation and to carry out other business pertaining to the Fellowship and Fellows, past, present, and future.

Section 8. The Editorial Board shall be appointed by the Editor, subject only to the approval of the Council. The Editor shall be, *ex officio*, the chairman of this board and shall be privileged to appoint and indefinitely reappoint such members of the Association, regardless of class of membership, and such non-members of the Association as in his opinion may be best calculated to meet the editorial requirements of the Association.

Section 9. The Ethics Committee shall consist of five members appointed by the Council. No member shall serve more than four years. The Ethics Committee shall advise the Council concerning alleged breaches of ethics. Complaints regarding alleged breaches of ethics shall be received in writing by the Ethics Committee and shall be investigated by it. In addition, the Ethics Committee may investigate on its own initiative.

Section 10. The Committee on Manpower shall be a Joint Committee of this Association and The Society of Thoracic Surgeons. The Committee shall consist of two members of this Association, two members of The Society of Thoracic Surgeons, and a Chairman who shall be a member of this Association and The Society of Thoracic Surgeons. The duties of this Committee, and the manner of appointment and term of its members and chairman, shall be determined jointly by the Council of this Association and the Council of The Society of Thoracic Surgeons.

Section 11. The Committee on Graduate Education in Thoracic Surgery shall consist of five members appointed by the Council. One member shall be appointed each year for a five-year term. The committee shall review graduate medical education in thoracic surgery and makes its recommendations to the Council to assist in meeting the educational mission of the Association.

## **ARTICLE VII. Finances**

Section 1. The fiscal year of the Association shall begin on the first day of January and end on the last day of December each year.

Section 2. Members shall contribute to the financial maintenance of the Association through initiation fees, annual dues, and special assessments. The amount of the annual dues and the initiation fees shall be determined by these By-Laws. If, at the end of any fiscal year, there is a deficit in the current funds of the Association, the Council may send out notices to that effect and invite Active members to contribute the necessary amount so that no deficit is carried over from one fiscal year to another. The Association may, in any regularly convened meeting, vote a special assessment for any purpose consistent with the purposes of the Association, and such special assessment shall become an obligatory charge against the classes of members affected thereby.

Section 3. To meet the current expenses of the Association, there shall be available all revenue derived by the Association subject to the provisions of Section 4, following.

Section 4. Funds derived from the payment of initiation fees shall not be available to current expenses and shall be placed in a special fund, to be invested and reinvested in legal securities, to be held intact, and to be known as the Endowment Fund. The Council is responsible for the proper management of the Endowment Fund, and may divert any surplus in the current funds of the Association into this fund, but may not withdraw any of the principal of the Endowment Fund except in accordance with the provisions of Section 6, following.

Section 5. The income from the Endowment Fund shall be expended as the Council directs.

Section 6. The principal of the Endowment Fund may be withdrawn, in whole or in part, under the following conditions only: The amount of principal to be withdrawn shall have been approved by the Council; it shall have been approved by a majority of the members present and voting at a regularly convened annual meeting; it shall have been tabled for one year; it shall have been finally passed by a three-fourths vote of the members present and voting at the next regularly convened annual meeting.

Section 7. In the event of the dissolution of the Association, the Endowment Fund shall be distributed among national institutions of the United States and Canada in a proportion equal to the then existing ratio between the numbers of citizens of the two nations who are members of the Association.

### **ARTICLE VIII. Meetings**

Section 1. The time, place, duration, and procedure of the annual meeting of the Association shall be determined by the Council and the provisions of the By-Laws.

Section 2. Notice of any meeting of the Association shall be given to each member of the Association not less than five nor more than forty days prior to any annual meeting and not less than thirty nor more than forty days prior to any special meeting by written or printed notice delivered personally or by mail, by or at the direction of the Council, the President or the Secretary. Such notice shall state the place, day and hour of the meeting and in the case of a special meeting shall also state the purpose or purposes for which the meeting is called.

Section 3. A special meeting of the Association may be called by the Council or on the written request of fifteen members delivered to the Council, the President or the Secretary. The specific purposes of the meeting must be stated in the request.

Section 4. Attendance at annual meetings and participation in the scientific programs shall be optional for all Honorary and Senior Members, but it shall be expected from all Active Members.

Section 5. Each annual meeting shall have at least two executive sessions.

Section 6. When the Association convenes for its annual meeting, it shall immediately go into the first executive session, but the business at this session shall be limited to:

1. Appointment of necessary committees.
2. Miscellaneous business of an urgent nature.

Section 7. The second executive session of the Association shall be held during the afternoon of the second day of the meeting. The business at this session shall include, but is not limited to:

1. Reading or waiver of reading of the minutes of the preceeding meetings of the Association and the Council.
2. Report of the Treasurer of the last fiscal year.
3. Audit Report.
4. Report of the Necrology Committee.
5. Report of the Program Committee.
6. Action on amendments to the Articles of Incorporation and By-Laws, if any.
7. Action on recommendations emanating from the Council.
8. Unfinished Business.

9. New Business.
10. Report of the Membership Committee.
11. Election of new members.
12. Report of the Nominating Committee.
13. Election of officers.

Section 8. Except where otherwise required by law of these By-Laws, all questions at a meeting of the members shall be decided by a majority vote of the members present in person and voting. Voting by proxy is not permitted.

Section 9. Fifty voting members present in person shall constitute a quorum at a meeting of members.

Section 10. While the scientific session of the annual meeting is held primarily for the benefit of the members of the Association, it may be open to non-members who are able to submit satisfactory credentials, who register in a specified manner, and who pay such registration fee as may be determined and published by the Council from year to year.

Section 11. There shall be an annual meeting of the Council held during the annual meeting of the Association. Additional meetings of the Council may be called on not less than seven days' prior written or telephonic notice by the President, the Secretary or any three members of the Council.

Section 12. Five members of the Council shall constitute a quorum for the conduct of business at any meeting of the Council, but a small number may adjourn any such meeting.

Section 13. Whenever any notice is required to be given to any member of the Council, a waiver thereof in writing, signed by the member of the Council entitled to such notice, whether before or after the time stated therein, shall be deemed equivalent thereto.

Section 14. Any action which may be or is required to be taken at a meeting of the Council may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the members of the Council. Any such consent shall have the same force and effect as a unanimous vote at a duly called and constituted meeting.

#### **ARTICLE IX. Indemnification and Directors and Officers**

Section 1. The Association shall indemnify any and all of its Councilors (hereinafter in this Article referred to as "directors") or officers or former directors or officers, or any person who has served or shall serve at the Association's request or by its election as a director or officer of another corporation or association, against expenses actually and necessarily incurred by them in connection with the defense or settlement of any action, suite or proceeding in which they, or any of them, are made parties, or a party, by reason of being or having been directors or officers or a director or officer of the Association, or of such other corporation or association, provided, however, that the foregoing shall not apply to matters as to which any such director or officer or former director or officer or person shall be adjudged in such action, suit or proceeding to be liable for willful misconduct in the performance of duty or to such matters as shall be settled by agreement predicated on the existence of such liability.

Section 2. Upon specific authorization by the Council, the Association may purchase and maintain insurance on behalf of any and all of its directors or officers or former directors or officers, or any person who has served or shall serve at the Association's request or by its election as a director or officer of another corporation or association, against any liability or settlement based on asserted liability, incurred by them by reason of being or having been directors or officers as a director or officer of the Association or of such other corporation or association, whether or not the Association would have the power to indemnify them against such liability or settlement under the provisions of Section 1.

#### **ARTICLE X. Papers**

Section 1. All papers read before the Association shall become the property of the Association. Authors shall leave original copies of their manuscripts with the Editor or reporter, at the time of presentation, for consideration for publication in the official Journal.

Section 2. When the number of papers makes it desirable, the Council may require authors to present their papers in abstract, and may set a time limit on discussions.

### **ARTICLE XI. Initiation Fees, Dues and Assessments**

Section 1. Honorary Members of the Association are exempt from all initiation fees, dues, and assessments.

Section 2. Annual dues for Active Members shall be \$150.00 and shall include a year's subscription to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Section 3. Senior Members are exempt from dues.

Section 4. The initiation fee for those elected directly to Active Membership shall be \$100.00.

Section 5. Active Members must subscribe to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY to retain their membership status.

Section 8. Subscription to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY is optional for Senior Members.

Section 9. Bills for membership dues and for subscriptions to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY will be mailed to members by the Treasurer after the Annual Meeting.

### **ARTICLE XII. Parliamentary Procedure**

Except where otherwise provided in these By-Laws or by law, all parliamentary proceedings at the meetings of this Association and its Council and committees shall be governed by the then current *Sturgis Standard Code of Parliamentary Procedure*.

### **ARTICLE XIII. Amendments**

Section 1. These By-Laws may be amended by a two-thirds vote of the members present and voting at an executive session of a properly convened annual or special meeting of the Association provided that the proposed amendment has been moved and seconded by not less than three members at a prior executive session of that meeting or a prior meeting of the Association.

Section 2. These By-Laws may be suspended in whole or in part for a period of not more than twelve hours by a unanimous vote of those present and voting at any regularly convened meeting of the Association.

As amended, Tuesday, April 27, 1993

## **Meetings of the American Association for Thoracic Surgery**

1918-Chicago.....	President, Samuel J. Meltzer
1919-Atlantic City.....	President, Willy Meyer
1920-New Orleans.....	President, Willy Meyer
1921-Boston.....	President, Rudolph Matas
1922-Washington.....	President, Samuel Robinson
1923-Chicago.....	President, Howard Lilienthal
1924-Rochester, Minn.....	President, Carl A. Hedblom

1925-Washington..... President, Nathan W. Green  
1926-Montreal..... President, Edward W. Archibald  
1927-New York..... President, Franz Torek  
1928-Washington..... President, Evarts A. Graham  
1929-St. Louis..... President, John L. Yates  
1930-Philadelphia..... President, Wyman Whittemore  
1931-San Francisco..... President, Ethan Flagg Butler  
1932-Ann Arbor..... President, Frederick T. Lord  
1933-Washington..... President, George P. Muller  
1934-Boston..... President, George J. Heuer  
1935-New York..... President, John Alexander  
1936-Rochester, Minn..... President, Carl Eggers  
1937-Saranac Lake..... President, Leo Eloesser  
1938-Atlanta..... President, Stuart W. Harrington  
1939-Los Angeles..... President, Harold Brunn  
1940-Cleveland..... President, Adrian V. S. Lambert  
1941-Toronto..... President, Fraser B. Gurd  
1944-Chicago..... President, Frank S. Dolley  
1946-Detroit..... President, Claude S. Beck  
1947-St. Louis..... President, I. A. Bigger  
1948-Quebec..... President, Alton Ochsner  
1949-New Orleans..... President, Edward D. Churchill  
1950-Denver..... President, Edward J. O'Brien  
1951-Atlantic City..... President, Alfred Blalock  
1952-Dallas..... President, Frank B. Berry  
1953-San Francisco..... President, Robert M. Janes  
1954-Montreal..... President, Emile Holman  
1955-Atlantic City..... President, Edward S. Welles  
1956-Miami Beach..... President, Richard H. Meade  
1957-Chicago..... President, Cameron Haight  
1958-Boston..... President, Brian Blades



1959-Los Angeles..... President, Michael E. De Bakey  
1960-Miami Beach..... President, William E. Adams  
1961-Philadelphia..... President, John H. Gibbon, Jr.  
1962-St. Louis..... President, Richard H. Sweet (Deceased 1-11-62)  
..... President, O. Theron Clagett  
1963-Houston..... President, Julian Johnson  
1964-Montreal..... President, Robert E. Gross  
1965-New Orleans..... President, John C. Jones  
1966-Vancouver, B. C..... President, Herbert C. Maier  
1967-New York..... President, Frederick G. Kergin  
1968-Pittsburgh..... President, Paul C. Samson  
1969-San Francisco..... President, Edward M. Kent  
1970-Washington, D. C..... President, Hiram T. Langston  
1971-Atlanta..... President, Thomas H. Burford  
1974-Las Vegas..... President, Lyman A. Brewer, III  
1975-New York..... President, Wilfred G. Bigelow  
1976-Los Angeles..... President, David J. Dugan  
1977-Toronto..... President, Henry T. Bahnson  
1978-New Orleans..... President, J. Gordon Scannell  
1979-Boston..... President, John W. Kirklin  
1980-San Francisco..... President, Herbert Sloan  
1981-Washington, D.C..... President, Donald L. Paulson  
1982-Phoenix, Arizona..... President, Thomas B. Ferguson  
1983-Atlanta..... President, Frank C. Spencer  
1984-New York..... President, Dwight C. McGoan  
1985-New Orleans..... President, David C. Sabiston  
1986-New York..... President, James, R. Malm  
1987-Chicago..... President, Norman E. Shumway  
1988-Los Angeles..... President, Paul A. Ebert  
1989-Boston..... President, W. Gerald Austen  
1990-Toronto..... President, F. Griffith Pearson

1991-Washington, D.C..... President, Keith Reemtsma  
 1992-Los Angeles..... President, John A. Waldhausen  
 1993-Chicago..... President, John L. Ochsner

## AWARDS

Back to Annual Meeting Program

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### GRAHAM EDUCATION AND RESEARCH FOUNDATION

13 Elm Street, Manchester, Massachusetts 01944, (508) 526-8330

President James L. Cox, M.D., St. Louis, Missouri  
 Vice President William A. Gay, Jr., M.D., New York, New York  
 Secretary-Treasurer William T. Maloney, Manchester, Massachusetts  
 Director G. Alec Patterson, M.D., St. Louis, Missouri

### EVARTS A. GRAHAM MEMORIAL TRAVELING FELLOWSHIP

The Evarts A. Graham Memorial Traveling Fellowship was established in 1951 by The American Association for Thoracic Surgery. Administered through the Graham Education and Research Foundation, it provides grants to young surgeons from North America and abroad who have completed their formal training in general, thoracic, and cardiovascular surgery. The award allows the recipient to study a year to intensify his training in a program of special interest and to travel to several sites to broaden his overall training and increase his contacts with thoracic surgeons internationally. Awards are made to surgeons of unique promise who have been regarded as having potential for later international thoracic surgical leadership. Since the inception of the Graham Fellowship, 42 young surgeons from 23 countries have completed their training at thoracic surgical centers.

1st	1951-52	L.L. Whythead, M.D., F.R.C.S. 790 Sherbrooke St., Winnipeg, Manitoba, R3A 1M3 CANADA
2nd	1953-54	W.B. Ferguson, M.B., F.R.C.S. Royal Victoria Infirmary, Newcastle-upon-tyne, ENGLAND
3rd	1954-55	Lance L. Bromley, M.Chir., F.R.C.S. St. Mary's Hospital, London, W.2, ENGLAND
4th	1955-56	Raymond L. Hurt, F.R.C.S. The White House, 8 Room Lane, Radlett Herts, ENGLAND
5th	1956-57	Mathias Paneth, F.R.C.S. Brompton Hospital, London, S.W. 3, ENGLAND
6th	1957-58	Peter L. Brunnen, F.R.C.S. Department of Thoracic Surgery, Woodend General Hospital, Aberdeen, SCOTLAND
7th	1958-59	N.G. Meyne, M.D. University of Amsterdam, Wilhelmina-Gasthuis, Amsterdam, HOLLAND
8th	1960-61	Godrej S. Karai, M.D. Calcutta, INDIA
9th	1961-62	Fritz Helmer, M.D. Second Surgical Clinic, University of Vienna, Vienna AUSTRIA
10th	1962-63	Theodor M. Scheinin, M.D. Tammisalonite 20, Helsinki, 00830, Finland
11th	1963-64	Masahiro Saigusa, M.D. National Nakano Chest Hospital, 3-14-20 Egata, Nakano-Ku, Tokyo 165, JAPAN
12th	1963-64	Adar J. Hallen, M.D.

- Department of Thoracic Surgery, University Hospital, Uppsala, SWEDEN
- 13th 1964-65 Stuart C. Lennox, M.D. 18 Alexander Sq., 5W3 2AX, London, ENGLAND
- 14th 1964-65 Elias Carapistolis, M.D., F.A.C.S.  
University Hospital Surgical Clinic, Aristote University of Thessolniki, Thessaloniki, GREECE
- 15th 1965-66 Gerhard Friehs, M.D.  
Chirurgische University Klinik, Graz A-8036, AUSTRIA
- 16th 1965-66 Ary Blesovsky, M.D.  
London, ENGLAND
- 17th 1966-67 C. Peter Clarke, F.R.A.C.S  
Ste. #4, 6th Floor, 55 Victoria Parade, Fitzroy 3065 AUSTRALIA
- 18th 1966-67 G.B. Parulkar, M.D.  
Wookhardt Heart Institute, Poonam Chambers B, A A Road, Bombay 400 018, INDIA
- 19th 1967-68 Claus Jessen, M.D.  
Surg. Dept. D, Rigshospitalet, Blegdamsvej 9, Copenhagen, DENMARK
- 20th 1969-70 Peter Brueke, M.D.  
AM Steinbruch, 29 Linz-Puchenau, A-4040, AUSTRIA
- 21st 1970-71 Michel S. Slim, M.D.  
New York Medical College, Division of Pediatric Surgery  
New York, New York 10595 USA
- 22nd 1971-72 Severi Pellervo, Mattila, M.D.  
Forsellesintie 5.7.D, Kaunianen, 02700, FINLAND
- 23rd 1972-73 Yasuyuki Fujiwara, M.D.  
Department of Cardiovascular Surgery, Tokyo Medical College  
Hospital, Shinjuko, Tokyo, JAPAN
- 24th 1973-74 Marc Roger de Leval, M.D.  
Hospital for Sick Children, Great Ormond Street., London, WC1N 3JH, ENGLAND
- 25th 1974-75 J. J. DeWet Lubbe, M.D.  
1406 City Park Medical Center, 181 Longmarket St., Cape Town 8001, REPUBLIC OF SOUTH AFRICA
- 26th 1975-76 Mieczyslaw Trenkner, M.D.  
Institute of Surgery, 80-211 U1, Deinsky 7, Gdansk, POLAND
- 27th 1976-77 Bum Koo Cho, M.D.  
Yonsei University, P.O. Box 71 Severance Hospital, Seoul, KOREA
- 28th 1977 -78 Alan William Gale, M.D.,FRACP, FRACS  
171 Sutherland, Paddington 2021, Sydney, AUSTRALIA
- 29th 1978-79 Eduardo Otero Goto, M.D.  
Servicio de Cirugia Cardiovascular, Ciudad Sanitaria "Le Fe", Valencia, SPAIN
- 30th 1980-81 Richard K. Firmin, M.D.  
"Moss Grove," 5 Knighton Grange Road, Stoneygate, Leicester LE2 2LF, ENGLAND
- 31st 1981-82 Claudio A. Salles, M.D.  
Av Celco Porfirio Machado, 370, Bairro Belvedere  
Belo Horizonte MG, BRAZIL
- 32nd 1982-83 Yasuhisa Shimazaki, M.D.  
First Dept. of Surgery, Osaka University Medical School  
Fukushima-ku, Osaka, 533, JAPAN
- 33rd 1983-84 Georg S. Kobinia, M.D.  
LKH Klagenfurt St., Veider Strasse 47, Dept. of Cardiac Surgery,  
Klagenfurt, A-9026, AUSTRIA
- 34th 1984-85 Aram Smolinsky, M.D.  
Department of Cardiac Surgery, The Sheba Medical Center  
Tel Hashomer, 52621, ISREAL
- 35th 1985-86 Florentino J. Vargas, M.D.  
San Martin 1353, Buenos Aries, ARGENTINA

36th	1986-87	Ari L. J. Harjula, M.D. Helsinki University Hosp. Surgery, Haartmanninkatu, Helsinki, 00290, FINLAND
37th	1987-88	Byung-Chul Chang, M.D. Dept. of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, CPo Box 8044, Seoul, KOREA
38th	1988-89	Wang Cheng, M.D. Department of Cardiac Surgery, Beijing Heart, Lung, Blood Vessel Medical Center and Anzhen Hospital, Andingmenwai, Beijing, PEOPLE'S REPUBLIC OF CHINA
39th	1989-90	Christopher John Knott-Craig, M.D. University of Oklahoma, Thoracic and Cardiovascular Surgery, P.O. Box 26901, Oklahoma City, OK 73190, USA
40th	1991-92	Ko Bando, M.D., Ph.D. Mayo Clinic, 200 Front Street SW, Rochester, MN 55905
41st	1992-93	Timothy E. Oaks, M.D. Department of Surgery, The Milton S. Hershey Medical Center, Room #6314, Box 850, Hershey, PA 17033, USA
42nd	1993-94	Alain E. Serraf, M.D. Hôpital Marie-Lannelongue, Université Paris Sud, 133, avenue de la Résistance, 92350 Le Plessis Robinson, FRANCE

## AWARDS

### 1993 FOUNDATION AWARDS

#### NINA S. BRAUNWALD RESEARCH FELLOWSHIP

Jennifer Dale Walker, M.D., Medical University of South Carolina

Dr. Walker is a third-year resident in general surgery, whose thesis concerns the evaluation of the thyroid hormone triiodothyronine, which has been shown to improve the left ventricular pump function. It has been suggested that T3 may have potential therapeutic value for patients with LV dysfunction. The use of thyroid hormone may have particular clinical importance with respect to cardiothoracic surgery, where the number of elderly patients with advanced cardiac disease and patients undergoing reoperation have continued to increase. This research proposal provides a logical and concise progression of basic research studies of the potential for using thyroid hormone as an inotropic agent as well as the basic mechanisms of its actions. A cardiothoracic laboratory at the University has focused upon the relationship of myocyte structure and function to overall ventricular performance. Accordingly, a specific objective of this will be to define the direct effects of thyroid hormone upon myocyte structure and contractile performance. A second objective of this project will be to determine the direct effects of acute thyroid hormone administration upon myocyte function following hypothermic cardioplegic arrest.

#### THE THORACIC SURGERY FOUNDATION RESEARCH FELLOWSHIP

Julie R. Glasson, M.D., Stanford University Medical Center

Dr. Glasson is a second-year resident in general surgery, whose project addresses "severing the chordae tendineae during mitral valve replacement [which] has been shown to have deleterious effects of cardiac function. We plan to investigate novel mechanisms responsible for this observation. We will also study alterations in the biochemistry of cardiac muscle as left ventricular function changes over time following mitral valve replacement. The results of this study will provide an understanding of the role of the mitral valve apparatus, both in maintaining LV function in normal hearts and in improving LV function in abnormal hearts with chronic mitral regurgitation

following mitral valve replacement. We expect to find that role to be a significant one, involving complex geometric alteration in the shape of the LV. At the conclusion of this project, we hope to discover a scientific rationale for utilizing chordal-sparing techniques during MVR and to provide a better understanding of the mechanisms by which the LV compensates for chronic mitral regurgitation."

#### **THE AMERICAN ASSOCIATION FOR THORACIC SURGERY RESEARCH SCHOLARSHIP**

The American Association for Thoracic Surgery Research Scholarship was established by the Association in 1985. Funded by the Association and individual contributions, the Research Scholarship provides opportunity for research, training and experience for North American surgeons committed to pursuing an academic career in cardiothoracic surgery. Administered by the Graham Education and Research Foundation, the program is undertaken within the first three years after completion of an approved cardiothoracic residency and is about two years in duration.

#### **EDWARD D. CHURCHILL RESEARCH SCHOLARSHIP**

##### **"Pharmacology of the Pulmonary Lymphatics"**

1986-1988 Mark K. Ferguson, M.D.

University of Chicago, Department of Surgery

#### **ALFRED BLALOCK RESEARCH SCHOLARSHIP**

##### **"Efficacy and Toxicity of a New Blood Substitute: Polymerized, Ultra-Pure, Stroma-Free Bovine Hemoglobin"**

1988-1990 Gus J. Vlahakes, M.D.

Massachusetts General Hospital and Harvard Medical School

#### **JOHN H. GIBBON, JR., RESEARCH SCHOLARSHIP**

##### **"Load-Independent Assessment of Cardiac Performance by Noninvasive Means"**

1990-1992 Donald D. Glower, M.D.

Duke University Medical Center

#### **ALTON OCHSNER RESEARCH SCHOLARSHIP**

##### **"Experimental Cardiac Graft Arteriosclerosis: Pathogenesis and Prevention of Lesion Development"**

1992-1994 David H. Adams, M.D.

Brigham and Women's Hospital

#### **ROBERT E. GROSS RESEARCH SCHOLARSHIP**

##### **"Role of Intra-Cellular Messenger cAMP and cGMP in Organ Preservation"**

1994-1996 Mehmet C. Oz., M.D.

Columbia-Presbyterian Medical Center

**"Development of a Model of Chronic Pulmonary Rejection in Miniature Swine"**

1994-1996 Thoralf Mauritz Sundt, III, M.D.

Washington University School of Medicine