
*PEDIATRIC HEART TRANSPLANTATION
PROTOCOL*

Revised June 2002

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TABLE OF CONTENTS

Pediatric cardiac transplantation: Introduction.....	1
PRE-OPERATIVE CARE: RECIPIENT	
Recipient inclusion criteria.....	3
Cardiac malformations in early infancy which have been considered for orthotopic transplantation.....	4
Recipient exclusion criteria.....	5
Care of cardiac transplantation candidates with ductal-dependent lesions.....	6
Work-up in histocompatibility laboratory in Immunology Center.....	12
PRE-OPERATIVE CARE: DONOR	
Donor inclusion criteria.....	13
Donor exclusion criteria.....	16
Care of the potential donor.....	17
PERI-OPERATIVE CARE	
Donor peri-operative protocol.....	18
Donor/recipient peri-operative management.....	18
Infectious diseases guidelines.....	19
Blood bank guidelines.....	21
Perfusion guidelines.....	21
Recipient peri-operative protocol.....	22
Anesthesia guidelines.....	23
Transport management.....	25
Operative method of transplantation.....	26
POST-OPERATIVE CARE	
Post-operative management.....	31
Posttransplant treatments and medications.....	31
Clinical signs of graft rejection.....	34
Rejection treatment guidelines.....	35
Discharge medications.....	36
Management of long-term immunosuppression.....	36
Outpatient follow-up: frequency of visits.....	36
Long-term follow-up guidelines.....	36
Information management.....	36
Recommended outpatient testing schedule.....	37
Routine pediatric care.....	39
Outpatient infectious diseases guidelines.....	39
Dental care guidelines.....	40
Guidelines for invasive follow-up studies.....	40
Indications for retransplantation.....	41
Protocol for pediatric heart transplantation autopsies.....	42

TABLE OF CONTENTS cont.

APPENDIXES

Administrative commitment.....	47
Pre-transplant evaluation check list.....	48
Cardiac transplant recipient evaluation worksheet.....	49
Intake information for potential heart transplant recipient (fetus).....	50
Intake information for potential heart transplant recipient (neonate).....	51
Intake information for potential heart transplant recipient (child).....	53
Social service expertise and commitment.....	57
Finances.....	57
Informed consent for recipient registration for heart transplantation.....	58
Cardiac donor checklist.....	60
Neonatal/pediatric pre-cardiac surgery physician order sheet.....	61
Operative note: Organ procurement/donor.....	62
Cardiac transplant nurse coordinator operating room protocol.....	63
In-house cardiac procurement operating room protocol.....	65
Distant cardiac procurement operating room protocol.....	67
Cardiac procurement scrub nurse duties and responsibilities.....	69
Cardiac procurement circulating nurse duties and responsibilities.....	71
Physician post-operative order sheet (Pediatric cardiac surgery).....	72
Neonatal/pediatric post-cardiac transplantation physician orders.....	73
Donor recovery protocol when donor infant is transferred to LLUMC.....	74
Pediatric transplantation visitation guide.....	75
Family rooming-in.....	76
Daily flowsheet for follow-up care.....	77
Methotrexate treatment guidelines.....	78
Total lymphoid irradiation guidelines.....	82
Nashville Anti-thymocyte serum (ATS) prophylaxis protocol.....	83
Anti-thymocyte serum (ATS) prophylaxis orders.....	85
Anti-thymocyte serum (ATS) rescue orders.....	87
ATGAM order sheet.....	89
Solumedrol order sheet.....	91
Prostaglandin E-1 guidelines.....	92
Glomerular filtration rates - Normal ranges.....	92
Guidelines for Sandoglobulin (IVIG) infusion.....	93
Sandoglobulin (IVIG) infusion orders.....	94
Drugs that alter cyclosporine levels.....	95
Minimum blood volume requirements.....	96
Cardiac transplantation as treatment for children with lethal heart disease associated with asplenia.....	98
Quality assurance plan.....	99
Clinical pathway.....	103
List of publications.....	112

PEDIATRIC CARDIAC TRANSPLANTATION LOMA LINDA UNIVERSITY MEDICAL CENTER

June 2002

Introduction

Loma Linda University Medical Center (LLUMC) is a 789 bed tertiary medical center operated by the Seventh-day Adventist Church. The Medical Center is located on the campus of Loma Linda University, a private, Seventh-day Adventist university which enrolls over 3,000 students annually in its seven schools, including schools of medicine, dentistry, nursing, and pharmacy. In 1993, a new state-of-the-art 244 bed Children's Hospital was opened to serve children's unique healthcare needs.

The Medical Center is the centerpiece of Loma Linda University Adventist Health Sciences Center, which also owns the Behavioral Medicine Center, a free-standing 89 bed psychiatric hospital. LLUAHSC comprises one of the four major divisions of Adventist Health System/US which operates 50 hospitals throughout the nation. Loma Linda University Medical Center is, however, governed locally by its own board of trustees and operates as a not-for-profit corporation.

The Medical Center is licensed by the State of California and accredited by the Joint Commission on Accreditation of Hospitals and Health Organizations. Loma Linda University Medical Center is approved by Health Care Financing Administration as a Medicare provider--**Provider No. 050327**. The Medical Center clinical laboratory is licensed by the State of California Department of Health Services.

Loma Linda University Medical Center provides the only training and research oriented academic cardiovascular medical/surgical service available to the four Southern California inland counties--Inyo, Mono, Riverside, and San Bernardino--which comprise about one-fourth of the State's land area. Fully approved training programs in general and cardiothoracic surgery, internal medicine, cardiology, and pediatrics have existed for a number of years. More recently, the vascular surgical service has become one of only three fully-approved training programs in vascular surgery in the State of California. In addition, Loma Linda University Medical Center is the only state-designated Level 1 Trauma Center serving the four inland counties of Southern California. The Medical Center is the principal clinical affiliating hospital for the Loma Linda University School of Medicine.

Basic science research in renal and cardiac transplantation at Loma Linda University dates back to early 1968, just one year after the opening of the new Medical Center facility and its 96,000 square foot medical research wing. The early research spawned here at Loma Linda University Medical Center developed into an active clinical kidney transplantation program which continues today. Laboratory research in cardiac, pancreatic islet cell, and liver transplantation has become much intensified since 1975, resulting in active clinical transplant programs.

Kidney transplantation at Loma Linda University Medical Center began in 1967; corneal transplantation in 1977; combined kidney-pancreas in 1993; combined kidney-heart in 1993; liver transplantation in 1993 and stem cell transplantation in 1999.

Newborn cardiac transplantation has been studied in the Loma Linda University Medical Center cardiothoracic surgical research laboratory since the spring of 1978. To date, over 400 newborn goats have undergone orthotopic cardiac transplantation using size matched goat donors (allografts) and size matched pig and lamb donors (xenografts). The relative immaturity of newborn immune systems has been demonstrated by prolonged survival among control group animals receiving no medication following cardiac transplantation.

Since 1985, approximately 80 infant baboons have received the hearts of either Rhesus or African green monkeys (concordant xenografts) or pigs (discordant xenografts) in the orthotopic or heterotopic position. Encouraging long term survival rates (as long as 16 months in a baboon who received a heart from a Rhesus monkey, utilizing *tacrolimus* and *methotrexate* immunosuppression) in these xenograft models suggest promise for

this technique. Consecutive survival greater than one year with baboon recipients of Rhesus monkey hearts managed with *cyclosporine* and *methotrexate* is very encouraging.

Data from these experimental cardiac transplantation procedures performed in the research laboratories on infant goats and baboons demonstrated: 1) the feasibility of heart transplantation in newborns and young infants; 2) adequate graft and host development; 3) infant responsiveness to immunoregulative drugs; 4) host reproductive capacity; 5) long term exercise capacity and survival. These and other data have formed the matrix for the clinical application of cardiac transplantation therapy during early infancy.

Based upon this experience along with a great deal of unpublished data demonstrating significant immunological similarities between common olive baboons and the human newborn infant population, approval was obtained from the Loma Linda University Institutional Review Board and numerous other interested standing committees within Loma Linda University to begin careful clinical trials of cross-species orthotopic cardiac transplantation in neonates with hypoplastic left heart syndrome (HLHS). The first such trial was launched in October 1984 with the implantation of a baboon heart into a premature newborn girl dying of HLHS. Although she lived 20 days, prolonged survival was precluded by a strong ABH incompatibility. She died as a result of disseminated hemagglutination. Production of anti-H antibody stimulated by parent H-antigen on vascular endothelium of the ABH incompatible graft became her nemesis. She appeared to gradually develop antibody (either specific or cross-reactive) to her own circulating type O erythrocytes causing them to agglutinate intravascularly. Major histocompatibility (MHC) antigen reactivity between baboon donor and human newborn was an extremely weak immune axis 20 days posttransplant and did not appear to contribute to her death. She was, perhaps, an important milestone in the understanding and application of xenotransplantation during early infancy. Her greatest legacy, however, was to underscore the need for infant organ donation. The first successful newborn heart allotransplantation procedure (on an infant who was four days of age) was accomplished at Loma Linda University Medical Center just over one year later, on November 20, 1985. That child remains alive and well today.

Since then, the infant/pediatric cardiac allotransplant recipient population has shown steady growth at LLUMC. Medicare approval for cardiac transplantation at LLUMC was granted in 1995. Five year actuarial survival for neonates undergoing cardiac transplantation at LLUMC is 81%. Survival for all infant recipients is 74% at 5 years.

Management of children undergoing cardiac transplantation has followed reasonably strict guidelines as outlined in this protocol with only minor variations. This document represents the most recent revision of the pediatric heart transplantation protocol and is current as of June 2002.

RECIPIENT INCLUSION CRITERIA

1. Post-conceptual age greater than 36 weeks and current weight greater than 2000 gms.
2. Cardiac diagnoses considered for transplantation:
 - a. Hypoplastic left heart syndrome (HLHS) or other lethal congenital heart disease for which there is no standardized treatment. Functional HLHS has been defined as:
 - Primary Criteria:**
 - Hypoplastic or absent morphologic left ventricle (left ventricular end diastolic volume $< 20 \text{ ml/m}^2$)
 - Aortic valve hypoplasia, stenosis, or atresia (diameter $< 5 \text{ mm}$ in term infant $< 2500 \text{ gms.}$)
 - Mitral valve hypoplasia, stenosis, or atresia (diameter $< 8 \text{ mm}$ in term infant $< 2500 \text{ gms.}$)
 - Secondary Criteria:**
 - Ductus-dependent systemic circulation (exception: critical aortic stenosis with hypoplastic left ventricle)
 - Ascending aortic hypoplasia (diameter $< 5 \text{ mm}$)
 - Aortic arch hypoplasia
 - May include:**
 - Double-outlet right ventricle
 - Interrupted aortic arch
 - Atrioventricular septal defect (canal)
 - Anomalous pulmonary venous connection
 - Atrial isomerism
 - b. End stage cardiomyopathy (including failed palliative surgery) with any of the following supportive findings:
 - i. Progressive deterioration in left ventricular ejection fraction or functional status despite optimal medical therapy including digoxin, diuretics and maximized vasodilator therapy (including angiotensin converting enzyme inhibitors)
 - ii. Failure to grow, secondary to advanced heart failure
 - iii. Malignant ventricular arrhythmias uncontrolled by conventional antiarrhythmic therapy and/or automatic implantable cardioverter defibrillator
 - iv. Symptomatic heart failure requiring continuous inotropic or mechanical support
 - v. Documentation of a progressive rise in pulmonary vascular resistance that would be expected to preclude transplantation at a later date
3. Reasonably stable metabolic and hemodynamic status while receiving prostaglandin (*PGE-1*) and/or other supportive measures (cardiac inotropic drugs, mechanical ventilation, parenteral nutrition) allowing time for donor identification
4. Psychosocial evaluation:
 - a. The candidate should reside within 45 minutes traveling time from Loma Linda University Medical Center for a minimum of four to six months posttransplantation to assure careful follow-up
 - b. The candidate's family should be capable of long-term supportive care of the child and be able to support the medical needs of the child in follow-up
 - c. Lack of parental (custodial) alcohol and/or substance abuse
 - d. No documented parental (custodial) child abuse or neglect
 - e. Parent (custodian) with no cognitive/psychiatric impairment severe enough to limit comprehension of medical regimen
5. No active clinical infection (see infectious diseases guidelines)

RECIPIENT INCLUSION CRITERIA cont.

6. Acceptable neurologic evaluation. No major central nervous system (CNS) abnormalities or severe pre-existing CNS injury. Neurological evaluation may include assessment of head ultrasound/CT/MRI scan and/or EEG
7. Acceptable renal function:
 - a. If BUN > 30 mg/dl and creatinine > 1.0 mg/dl, pediatric nephrology consultation to exclude gross renal abnormalities
 - b. Abdominal/renal ultrasound study to exclude significant renal malformations
 - c. Preoperative isotopic GFR to assess baseline renal function may be required
8. No chromosomal abnormalities or syndromes which would seriously limit survival or perception of benefit from transplantation; may require genetic evaluation
9. Recipients with asplenia syndrome have not posed an increased risk following transplantation

CARDIAC MALFORMATIONS IN EARLY INFANCY WHICH HAVE BEEN CONSIDERED FOR ORTHOTOPIC TRANSPLANTATION

1. Hypoplastic left heart syndrome (hypoplastic aortic tract complex)
2. Hypoplastic left heart equivalent:
 - a. D-TGA with hypoplastic right ventricle and aortic tract
 - b. Single ventricle with hypoplastic aortic tract
 - c. L-TGA with single ventricle and heart block
 - d. Shone's complex -- severe mitral valve stenosis (atresia), left ventricular outflow obstruction, coarctation of the aorta
3. Symptomatic severe Ebstein's anomaly with normal pulmonary arteries
4. Multiple obstructive rhabdomyomas or fibromas
5. Pulmonary atresia/intact ventricular septum (large sinusoids*)
6. Severe congenital or acquired cardiomyopathy at end stage with maximal medical management
7. A-V canal with hypoplastic left ventricle and mitral component (frequently associated with coarctation)
8. Single ventricle with sub-aortic obstruction (bulbo-ventricular foramen)
9. Severe intrauterine A-V valve insufficiency and ventricular dysfunction (see #2 for L-transposition)
10. Straddling A-V valve and tensor apparatus
11. Complex truncus arteriosus

*Diminutive right heart malformations MUST have adequate-sized right and left pulmonary arteries. Neonates unresponsive to *PGE-1* may have systemic-pulmonary shunts while awaiting a donor.

RECIPIENT EXCLUSION CRITERIA

1. Marked prematurity and low birth weight which would limit access to cardiopulmonary bypass
2. Unclear cardiac diagnosis; although there is wide variability in the anatomic presentation of many potential recipients with congenital heart disease. **Only two absolute anatomic contraindications have been identified: absence or marked hypoplasia of central pulmonary arteries and absence or markedly diminutive pulmonary veins.**
3. Persistent acidosis with pH below 7.10
4. Active infection (see infectious diseases guidelines)
5. Abnormal neurological evaluation suggesting poor long-term prognosis which would significantly impair the patient's ability to consistently and reliably comply with the complex post-transplant medical regimen.
6. Abnormal renal function:
 - a. Significant urinary tract anomaly
 - b. Persistent renal failure or persistent marked reduction in renal function not likely to improve after increasing cardiac output after cardiac transplantation.
7. Significant genetic problem or syndrome or constellation of birth defects which would limit survival or potential benefit from transplantation

CARE OF CARDIAC TRANSPLANTATION CANDIDATES WITH DUCTAL-DEPENDENT LESIONS

Resuscitation and Initial Stabilization

Resuscitation and recovery from circulatory stresses may, or may not, be a major issue at presentation:

No or minimal impact if prenatal or very early diagnosis, allowing early intervention

Moderate to large impact if presentation includes systemic circulatory collapse as PDA constricts and restricts systemic perfusion

Basic concepts regarding resuscitation should be followed with special emphasis on circulation. If the infant exhibits circulatory compromise at presentation consider the following:

Volume resuscitation: Infants may be relatively hypovolemic from decreased intake and will certainly exhibit weak systemic perfusion. Administer liberal amounts of fluid to tolerance (until signs of increasing pulmonary edema and CHF)

Correction of acidosis: Acidosis may depress cardiac activity and increase systemic vascular resistance contributing to poor systemic perfusion even after ductus arteriosus constriction is treated with PGE₁. There may be substantial lactate buildup in poorly perfused tissues that will take time to clear even with restored circulation. Generous use of bicarbonate may improve rate of recovery of systemic circulation

Inotropic support: May be necessary until depressed cardiac function or acute CHF is controlled (also see discussion on cardiac support)

Avoid high FIO₂ and hypocarbia while treating hypoxia and acidosis (also see discussion on pulmonary support)

Initiation and Maintenance of PDA

PGE₁ is started at 0.05 mcg/kg/min.

PGE₁ is often decreased to 0.025 mcg/kg/min when PDA evaluated and found to be large and unrestrictive. May experience less apnea, jitteriness, and fever, acutely; and chronically, less periosteal bone changes and muscle hypertrophy

Rarely PGE₁ is increased to 0.10 mcg/kg/min when PDA evaluated and found to be small and restrictive. If a small, restrictive PDA is unresponsive to increased PGE₁, consider vascular stenting to enlarge and maintain PDA patency

PGE₁ dosage less than 0.025 mcg/kg/min considered only if substantial side-effects to a larger dose. PGE₁ never infused at less than 0.01 mcg/kg/min (generally not even in infants with PDA stents)

Regardless of rate of infusion, the rate should be fast enough to ensure adequate monitoring of rate of infusion and recognition of IV infiltration (minimum of 3 mL/hr with peripheral IV or 1 mL/hr with central IV). A second IV site should be available for other medications and as a back-up site in the event of failure of the in-use PGE₁ infusion site

CARE OF CARDIAC TRANSPLANTATION CANDIDATES WITH DUCTAL-DEPENDENT LESIONS cont.

Fluids/Nutrition

Liberal fluids will be administered to cardiopulmonary tolerance (beyond 160 mL/kg/day is rarely tolerated) unless managing sequelae of systemic circulatory shock with acute renal failure, capillary leak syndrome or neurologic insult

Most infants managed with a 100 - 140 mL/kg/day fluid intake

Fluids will be provided as enteral feedings of breast milk or standard formulas as tolerated. Remainder of fluids (if any) will be as PGE₁ infusion and TPN

Failure to grow at normal rates is one of the most common problems in the pretransplant period. Optimal nutritional support is an important determinant of strength and stability of an infant waiting for transplantation. As the length of this period is variable and frequently prolonged, earlier and more aggressive nutritional support intervention may improve survival and contribute to less morbidity in this patient population. Calorie intake and caloric density of feedings may need to be increased to offset low fluid limit or increased energy consumption

Cardiac Support

Unless cardiogenic shock, hypoxemia and acidosis are present at time of diagnosis, cardiac function is usually strong and can be maintained with minimal or no inotropic support. Cardiac support drugs that may be used individually or in combination to support cardiac output and systemic perfusion include:

Dobutamine (5-10 mcg/kg/min): improves contractility and systemic perfusion through inotropic and afterload reduction effects when inotropic support is needed for resuscitation

Dopamine (3-7 mcg/kg/min): low doses only to support renal perfusion and/or as an adjunct to *dobutamine* for supporting systemic perfusion, especially in the presence of hypotension

Digoxin (8-10 mcg/kg/day): may be used for chronic inotropic support in the infant with stable electrolytes, renal and GI function

Diuretics (e.g. *furosemide* 1.0 mg/kg/dose): may be used for pulmonary edema, fluid retention and mild CHF

ACE inhibitors may be used for low systemic perfusion states associated with normal or elevated blood pressure to reduce systemic vascular resistance and to increase distribution of cardiac output to the systemic circulation

Pulmonary Support

Early support may be necessary for resuscitation or treatment of mild pulmonary congestion and CHF

If intubated for resuscitation or CHF, infants are weaned and extubated as soon as possible (hours to days)

CARE OF CARDIAC TRANSPLANTATION CANDIDATES WITH DUCTAL-DEPENDENT LESIONS cont.

Infants dependent on the PDA for systemic blood flow should not be expected to maintain normal oxygen saturations. Expect %SatO₂ ideally to range from 80-85% which should reflect a near 1:1 ratio of not overly desaturated systemic venous return and 100% saturated pulmonary venous return

If oxygen desaturation predominates (%SatO₂ < 80%), this may represent a restrictive foramen ovale; or, if early in the course, possibly still high and reactive pulmonary vascular resistance

Occasionally infants will display %SatO₂ > 90% without signs of pulmonary overperfusion or CHF; this may represent preferential streaming of more desaturated RV output to the lungs and well saturated RV output to the body via the PDA. Not treated (with lowered FIO₂ < 0.21) unless there are signs of CHF

Supplemental oxygen should be used sparingly:

Increased FIO₂ will act as a pulmonary vasodilator increasing the distribution of cardiac output to the lungs creating a risk for pulmonary overcirculation. To maintain adequate systemic perfusion, cardiac output must increase which creates an increased risk for congestive heart failure. To reduce risks of increased FIO₂ consider the following:

If infant is intubated, preoxygenate with low FIO₂ (0.21-0.40 rather than 1.00) for suctioning and procedures

Do not transport without oxymetry monitoring

Do not transport with or use FIO₂ of 1.00 if infant needs ventilatory assistance during transport or procedures. Generally preferable to use 0.21 FIO₂ (self-inflating bag if no compressed air available)

Transient decreases in %SatO₂ below 80% are not treated with supplemental oxygen. Prolonged oxygen desaturation may be treated with increased FIO₂

When supplemental oxygen is required, evaluate potential causes which include:

pulmonary edema from pulmonary overperfusion

congestive heart failure

elevated systemic vascular resistance, or

some combination of these conditions

Treat with diuretics, fluid restriction, inotropic support, systemic afterload reduction or some combination of these treatments as indicated, rather than increasing FIO₂ requirement

Reevaluate for restrictive foramen ovale when FIO₂ requirement persists > 0.40 after treatment for pulmonary edema and/or congestive heart failure

Management of ventilation (pCO₂) and effects on pH:

Most infants with ductal-dependent lesions awaiting transplantation are tachypneic

Spontaneous ventilation may be increased because of central and peripheral chemoreceptor response to hypoxemia and/or CO₂ retention due to pulmonary edema and CHF

CARE OF CARDIAC TRANSPLANTATION CANDIDATES WITH DUCTAL-DEPENDENT LESIONS cont.

Increased ventilation may be associated with:

Low pCO₂ (absence of significant pulmonary edema and CHF)

Normal pCO₂ (mild pulmonary edema and CHF)

Increased pCO₂ (moderate to severe pulmonary edema and CHF)

Treat pulmonary edema and CHF when associated with moderately increased pCO₂ and moderate acidosis pH (< 7.30). Avoid alkalosis which may reduce pulmonary vascular resistance increasing risk for pulmonary edema, CHF and decreased systemic perfusion

Alkalosis may be caused by:

Over-ventilation with mechanical ventilatory support (including mask and bag ventilation for procedures). Avoid high ventilator rate or tidal volumes. Use PEEP (4-6 cm H₂O) to improve oxygenation with less risk for hypocarbia and alkalosis

Hypochloremic metabolic alkalosis may result from diuretic use

Contraction alkalosis may result from aggressive volume restriction

Lines/Monitoring/Daily Care

Arterial Lines

UA catheters are frequently placed to assist in stabilization and are the initial arterial access line of choice

Peripheral arterial lines may be used but will frequently require 2 mL/hr line infusion that will be either an additional fluid burden or will be relatively non-nutritive

In infants with little or no cardiorespiratory distress at presentation, an arterial line may not be placed. More than brief duration use of UA catheters may increase risk for:

Delayed introduction of feedings

Greater dependence on laboratory tests resulting in iatrogenic anemia and PRBC transfusions that could increase donor antigen exposure

Artery spasm

Line infections

Thrombus formation

Necrotizing enterocolitis

Intravenous Access

Anticipate need for prolonged intravenous access (before, during and after transplantation)

Maintain at least two (2) IV sites at all times: one site for PGE₁ infusion; and one site for other medications and/or as back-up site for PGE₁ infusion

Consider placement of a PICC line early using small bore sialastic catheters to reduce risk of thrombosis. Infectious complications with PICC lines are no greater than with surgically inserted central lines (e.g. Broviac catheters) with careful management and protection of insertion site

CARE OF CARDIAC TRANSPLANTATION CANDIDATES WITH DUCTAL-DEPENDENT LESIONS cont.

Surgically inserted central lines or CVP lines in neck or groin are avoided due to greater risk of central thrombus, mechanical problems and infection

Routine Evaluations

Physical assessment:

General state: Including: respiratory rate, %SatO₂, weight change, intake and output, tolerance of feedings

Cardiac status: Sufficiency of circulation and signs of CHF, including: BP, pulses, color, warmth of extremities

Pulmonary status: Rate and effort of breathing, rales

Ancillary Tests:

Chest radiographs: Obtain at least weekly. Increasing heart size generally correlates with decreasing pulmonary vascular resistance, increasing proportion of cardiac output to lungs and CHF. Decreasing heart size with persistent interstitial pulmonary edema suggests restrictive foramen ovale

Echocardiogram: Obtain weekly and as necessary. Frequency may be reduced if quite stable. Evaluate cardiac function, status of PDA and foramen ovale

Blood culture and CBC: Obtain at least weekly and as necessary for evaluation of secondary infection. Goal is to facilitate early recognition and treatment of any suspected infection. Only actively infected patients are withheld from transplantation. Antibiotics should be withdrawn if infection disproved over time

Chemistry Profile: Obtain weekly to evaluate electrolytes, BUN and creatinine for signs of adequate volume, electrolyte support, renal function and to evaluate nutritional status and tolerance of TPN

Psychosocial Intervention

From a stress and psychological perspective, the pretransplant period is the most difficult period of the transplant process for most parents

Frequent communication of status and encouraging parental involvement with care may ease stress and facilitate bonding

Mortality Risk and Associations

There is a significant mortality risk in the pretransplant period:

25% of all HLHS infants registered for transplantation will die waiting for a donor; approximately 14% in the first 30 days, 9% after 1-2 months, and approximately 1% per month thereafter

CARE OF CARDIAC TRANSPLANTATION CANDIDATES WITH DUCTAL-DEPENDENT LESIONS cont.

Causes of early death are generally related to:

Asphyxia at time of presentation/diagnosis if ductal-dependent lesion not identified prior to substantial constriction of the PDA

Highly restrictive foramen ovale with severe respiratory failure with/without severe pulmonary hypertension

Ductus arteriosus constriction unresponsive to PGE₁

Causes of later death are generally related to:

Congestive heart failure

Infectious complications

Necrotizing enterocolitis

Secondary organ system failure(s) -- most notably kidney failure and CNS damage

Changes in status that are expected to affect survival to transplantation, survival of the transplantation surgery, and/or quality of life and health after transplantation are communicated to the family so they may continue to advocate for their child for the treatment option they are most comfortable pursuing including the withdrawal of support or palliation.

WORK-UP IN HISTOCOMPATIBILITY LABORATORY IN LLUMC IMMUNOLOGY CENTER

The following studies are obtained on potential recipients and donors:

A. Laboratory studies - Recipient

1. Pretransplantation

- a. Confirm ABO type (Blood Bank - pink top tube)
- b. Panel Reactive Antibody (PRA) as indicated
- c. Take history of presensitization events: # of transfusions (dates, type of blood products, if possible), any previous surgery or transplant, pregnancies, dates and types of

immunizations

2. At time of transplantation

- a. HLA - A, B, C, DR, DQ
- b. Donor specific antibody testing
- c. CFC Cardiac Transplant Profile
- d. Crossmatch donor lymphocytes (CDC)
- e. Donor Specific antibody testing (CDC)
- f. T cell flow cytometry crossmatch

B. Laboratory studies - Donor

- a. Confirm ABO type (Blood Bank)
- b. HLA - A, B, C, DR, DQ

C. After donor heart is recovered, collect lymph nodes and spleen on ice or place in refrigerator, and any available blood (up to 60 ml) in green top tubes and **keep at room temperature** for “donor-specific antigen”, which will be stored in liquid nitrogen in the Histocompatibility Lab of the Immunology Center.

DONOR INCLUSION CRITERIA cont.

4. An echocardiogram showing a structurally normal heart with “reasonable” cardiac function. Mild echocardiographic abnormalities in structure (e.g. PFO) or function may not disqualify a heart from consideration. In general, a left ventricular shortening fraction of > 25% is acceptable. The ejection fraction should be > 40%. Mitral regurgitation is a contraindication. Duration of cardiac arrest has not been a disqualifying factor in deciding whether to utilize a donor heart if cardiac function becomes adequate over time. Inotropic support and volume resuscitation may be required to improve cardiac function as a result of significant fluid restriction during cerebral resuscitation. The electrocardiogram should be essentially normal
5. ABO matched or compatible with potential recipient
6. Appropriately size-matched to potential recipient. Cautious use of infant donor smaller than recipient. Generally, donor hearts that are up to three times greater in weight than the recipient are considered feasible. Hearts from donors up to four times greater in weight have been accepted on rare occasions
7. Anencephaly - if above criteria for brain death have already been met as well as all other criteria
8. Sudden Infant Death Syndrome (SIDS) - not a contraindication to donation if cardiac function is satisfactory

*Apnea Test

- a) Deliver 100% O₂ for 10 minutes. Ventilate normally to allow pCO₂ to approximate 45-50 torr.
- b) Cease ventilation and observe for respiratory movements, usually for 10 minutes.
 - 1) Obtain several arterial blood samples to confirm that pCO₂ is >60 torr before resuming mechanical ventilation.
 - 2) Although the original description recommended disconnecting the ET tube from the ventilator and placing a catheter deep in the trachea to supply apneic oxygenation, there has been precedent from 1983 for keeping the patient attached to the ventilator and providing positive end expiratory pressure (PEEP) to avoid a precipitous fall in pO₂, with consequent drop in blood pressure and/or heart rate.
 - 3) Because of the phenomenon of hypoxic respiratory depression which occurs with neonates, some have advocated requiring the pO₂ to remain above 60 torr, but this is not required by the 1987 Task Force for The Determination of Brain Death in Children.

REFERENCES

1. Guidelines for the determination of death. Report of the medical consultants on the diagnosis of death to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. JAMA 1981; 246:2184-2186.
2. Report of Special Task Force. Guidelines for the determination of brain death in children. American Academy of Pediatrics Task Force on Brain Death in Children. Pediatrics 1987; 80:298-300.
3. President's Commission for the Study of Ethical Problems in Medicine and Biomedical Behavioral Research. Defining Death: A Report on the Medical, Legal, and Ethical Issues in The Determination of Death. Washington, D.C.: Government Printing Office, 1981.
4. Gervais KG. Redefining Death. New Haven: Yale University Press, 1986.
5. Veatch RM. Death, dying, and the biological revolution. New Haven, CT: Yale University Press, 1989.
6. Goldsmith J, Montefusco CM: Nursing care of the potential organ donor. Critical Care Nurse 1985; 5:22-29.

REFERENCES cont.

7. Kaufman HH, Lynn J: Brain death. *Neurosurgery* 1986; 19:850-856.
8. Ashwal S. Brain Death in the Newborn. *Clinics in Perinatology*, Vol. 16, No. 2, June, 1989.
9. Drake B, Ashwal S, Schneider S. Determination of cerebral death in the pediatric intensive care unit. *Pediatrics* 1986: 78:107-12.

DONOR EXCLUSION CRITERIA

1. Does not meet brain death criteria as outlined under Donor Inclusion Criteria
2. Anencephaly (unless brain death present and all other criteria are met)
3. Cardiac malformations other than:
 - a. Simple patent ductus arteriosus
 - b. Simple atrial septal defect
 - c. Trivial ventricular septal defect
 - d. Trivial semilunar valve abnormality
4. Evidence of severe myocardial ischemic injury: e.g.; poor ventricular function on echocardiography without improvement after volume replacement and appropriate inotropic support and/or:
 - a. Ejection fraction < 40%
 - b. Shortening fraction < 25%
 - c. Mitral regurgitation
5. Evidence of significant infection (see infectious diseases protocol)
 - a. Uncontrolled bacterial sepsis
 - b. HIV positivity, Hepatitis B Surface antigenemia
 - c. Hepatitis C positivity*
 - d. Untreated infection
6. ABO incompatibility with potential recipient
7. Inappropriate size match for potential recipient

* Relative exclusion criteria - information may not be available prior to transplant.

CARE OF THE POTENTIAL DONOR

Once brain death has been diagnosed, immediate attention must be given to the maintenance of organ function. Prolonged maintenance of a brain dead individual results in the deterioration of organ function primarily as a consequence of declining systemic perfusion. Adherence to an established donor monitoring protocol ensures that organs are recovered in optimal condition. The following guidelines are essential to such a protocol:

1. Maintenance of optimal tissue and organ perfusion
2. Maintenance of fluid and electrolyte balance
3. Maintenance of adequate blood gases
4. Prevention of secondary infection
5. Maintenance of normal temperature

Hemodynamic management is essential and hemodynamic status must be meticulously assessed if adequate perfusion of potential donor organs is to be maintained. Inotropic support may be necessary even after fluid loading is accomplished. Clinical management of a potential organ donor is often complicated by the hemodynamic instability associated with catecholamine fluxes that follow brain death, requiring the administration of inotropic support. Contributing to severe derangements in the hemodynamics of brain dead organ donors are fluctuations in body temperature, large fluid shifts due to the development of diabetes insipidus, and significant cardiac arrhythmias.

The development of diabetes insipidus is common after brain death as a result of the failure of the hypothalamus or posterior pituitary gland to produce or release antidiuretic hormone. The result is often an abnormally high output of very dilute urine, leading to hypovolemia, falling blood pressure, hemoconcentration and decreased systemic perfusion. This condition must be treated immediately with fluid replacement and with infusions of vasopressin in order to maintain adequate blood pressure.

Required documents

1. Brain death certified by two physicians. May be recorded on progress notes that document brain death according to state laws
2. Parents' consent for organ donation
3. Documentation of coroner's consent (if applicable)
4. Copy of donor medical record
5. Copy of echocardiogram videotape
6. Donor blood and tissue specimens for infectious diseases screen and tissue typing (procured on site)
7. Confirmation of blood type

DONOR PERIOPERATIVE PROTOCOL

1. If the donor is found to be satisfactory, supportive care is continued until the time of procurement
2. Donor and recipient are taken to adjacent operating rooms simultaneously (when donor is on site)
3. Heart (multi-organ) procurement is accomplished
4. Multiple lymph nodes, blood, and spleen are obtained (for processing in the Immunology Center)
5. Perioperative donor medications administered in the operating room by anesthesia include:

Solumedrol 125 mg IV

Heparin 5 mg/kg IV

Cefazolin 250 mg IV (unless otherwise specified)

50% *Dextrose* 5-10 cc every 15 minutes IV (slowly)

6. Roe's Solution for cardioplegia:
NaCl 27 mEq/l
KCl 20 mEq/l
Solumedrol 250 mg/l
MgSO₄ 3 mEq/l
D5W 1000 ml (kept in refrigerator
pH adjusted to 7.40 with *NaHCO₃* (2.25 mEq). Store in refrigerator. Do not pre-mix.
7. Graft stored in approximately 4° C normal saline (500cc to which 10cc of 50% *Dextrose* has been added)

DONOR/RECIPIENT PERIOPERATIVE MANAGEMENT

After diagnosis and general evaluation of any potential transplant candidate, the child is registered with United Network For Organ Sharing (UNOS). Every effort will be made to locate an ABO-type-specific (or compatible) size-matched human donor.

An infant or child accepted for transplantation at Loma Linda University Medical Center may be maintained in the referring facility and cared for by the referring neonatologist, pediatrician, or intensivist until a donor is identified. This is feasible only if immediate transfer of the recipient (within 6 hours of notification) can be accomplished by the referring facility. Upon donor notification, the recipient is transferred to LLUMC. All immediate preoperative assessment and management will then be administered by the cardiac surgical service, utilizing pediatric consultants as indicated. Should a potential recipient be transferred to Loma Linda while still awaiting a donor, that infant will be managed by the neonatology service in the neonatal intensive care unit (under 60 days of age), or by the pediatric transplant service and/or PICU service in the pediatric cardiac surgery ICU or general pediatric intensive care unit (children over 60 days of age).

Donor infants transported to Loma Linda University Medical Center will be evaluated and managed either by the neonatology service (infants under 60 days of age) or by the pediatric intensive care service (children over 60 days of age).

INFECTIOUS DISEASES GUIDELINES

1. Inclusion Criteria:
 - a. Recipient: No evidence of symptomatic infection
 - b. Donor: No evidence of symptomatic infection

2. Exclusion Criteria:
 - a. Recipient:
 - 1) Evidence of sepsis
 - 2) Symptomatic congenital viral infection* (relative)
 - 3) Hepatitis B surface antigenemia
 - 4) HIV positivity
 - 5) Hepatitis C positivity (relative)

 - b. Donor:
 - 1) Evidence of sepsis
 - 2) Symptomatic congenital viral infection*
 - 3) Hepatitis B surface antigenemia
 - 4) HIV positivity
 - 5) Hepatitis C positivity (relative- consider heart for Hepatitis C positive recipient only)

3. Criteria for delaying or canceling surgery - presence of one major or two minor clinical signs of sepsis in the recipient:
 - a. Major:
 - 1) WBC < 4000/mm³
 - 2) Absolute neutrophil count < 1000/mm³
 - 3) Temperature > 100°F. Ax. or < 97° using a cutaneous probe
 - 4) Shock
 - 5) Acidosis
 - 6) Cutaneous, soft tissue infection
 - 7) Pneumonia

 - b. Minor:
 - 1) Maternal fever > 101°F orally
 - 2) Odoriferous amniotic fluid
 - 3) WBC > 25000/mm³
 - 4) Hypoglycemia or hyperglycemia

*Symptomatic congenital viral infection:

- a. Clinical signs: small for gestational age, rash, hepatosplenomegaly, microcephaly, chorioretinitis
- b. Laboratory: neutropenia, thrombocytopenia, IgM > 20 mg/dl, Toxo IFA > 1/1024, actively shedding CMV (viral culture positive)
- c. Radiographic signs: abnormal cranial ultrasound or bone survey

INFECTIOUS DISEASES GUIDELINES cont.

4. Pretransplant infectious diseases screen
 - a. Recipient:
 - 1) CBC, platelet count
 - 2) CMV titers (IgG, IgM); EBV titers (EBV-IgG, EBV-IgM) (blood is stored for potential future use; actual testing is deferred.)
 - 3) HIV, Rapid Plasma Reagin or equivalent
 - 4) Hepatitis B Surface Antigen
 - 5) Hepatitis C antibody
 - 6) Radiograph of chest, kidneys, ureters and bladder
 - b. Donor:
 - 1) CMV titers (IgG, IgM), PCR
 - 2) HIV, Rapid Plasma Reagin or equivalent
 - 3) Hepatitis B Surface Antigen
 - 4) Hepatitis C antibody
 - 5) Bacterial cultures from endotracheal tube, urine and blood
 - 6) Toxoplasma PCR
 - 7) EBV PCR
5. Therapeutic intervention for infectious diseases
 - a. Sepsis - Pretransplantation
If hemodynamically stable, complete sepsis evaluation including:
 - 1) blood, urine, cerebrospinal fluid cultures
 - 2) followed by appropriate intravenous antibiotics
 - 3) delay surgery until negative culture results are availableIf hemodynamically unstable: immediate therapeutic intervention
Decision for surgery rests with cardiac surgeon, neonatologist/pediatrician, cardiologist, and infectious diseases specialist.
 - b. Cytomegaloviral infection
See CMV management per outpatient infectious diseases guidelines
6. Prophylactic antibiotics posttransplant, unless otherwise specified:
 - a. *Cefazolin* 20 mg/kg/dose every 12 hours (for infants from birth to one month of age);
25 mg/kg/dose every eight hours (for infants greater than one month of age)
 - b. Initial antibiotic dose immediately prior to commencement of surgery
 - c. Duration of postoperative administration is 48 hours or until invasive devices are removed
 - d. *Acyclovir* 15-30 mg/kg/day -- IV or orally TID for three months for low risk patients
 - e. *Ganciclovir* 5-10 mg/kg/day divided every 12 hours for 10-14 days for CMV negative recipients who receive a CMV positive donor organ. Dose adjusted for renal impairment
 - e. *Nystatin* orally TID for three months
7. All blood products should be leukopore filtered and irradiated
8. Posttransplantation infection control: Handwashing (3 minute scrub) or gloves are required. The child is cared for in an ICU room. The room may be shared by other patients who are known to be free from infection. Gowns and masks are not required. Caregivers should be free from known infections. Universal precautions should be in effect at all times.

BLOOD BANK GUIDELINES

Transplant recipients have special needs that require more care by the Blood Bank before blood products can be administered.

Preparing blood and blood products for transplantation may take up to six hours following notification of donor acquisition. Demands for a shorter turn-around time on all tests will depend on circumstances surrounding both recipient and prospective donor. The Blood Bank Supervisor will be notified by the Director of Immunology Service when a decision has been made to proceed with transplantation.

1. When ABO/Rh typing is completed, appropriate blood products are ordered from the San Bernardino/Riverside Counties Blood Bank
2. CMV Status:
Infant / pediatric recipients - receive CMV negative units only, (regardless of CMV status). Mother may require testing to determine if a positive CMV IgG titer in newborn is due to passive transfer of maternal antibody
3. The following blood products are ordered from the San Bernardino/Riverside Counties Blood Bank for infant and pediatric patients:
 - a. 3 units Platelet Concentrate
 - b. 4 units Fresh Frozen Plasma (FFP)
 - c. 6 units red blood cells (RBC's) that are CMV negative, leukocyte depleted and irradiated in the LLUMC Blood Bank
4. Red cell antibody screen and crossmatches are accomplished
5. All cellular blood products will be irradiated and leukodepleted by the Blood Bank

PERFUSION GUIDELINES*

Follow current perfusion protocol for newborn and infant cardiac surgery requiring profound hypothermia and circulatory arrest with the following exceptions:

1. All blood and blood products must have been irradiated prior to use and passed through a leukopore filter (check label)
2. *Methylprednisolone(Solumedrol)*: 20 to 25 mg/kg is administered via the circuit
2. Core cooling will be accomplished with temperature lowered to 16° core esophageal (lowest), aiming for 20° core rectal
3. During rewarming, titrate washed RBC's and FFP gradually into oxygenator when temperatures are between 22° and 30°C. Use hemoconcentrator to reduce overall circuit volume
4. Obtain serial ACT's, ABG's, electrolytes, and Hb throughout rewarming phase
5. Anticipated period of circulatory arrest is *50-60 minutes*

*Reference: International Practice in Cardiothoracic Surgery. (Eds) Yingkai Wand Peters RM. Scientific Press, Beijing, 1985; Ch. 15:135.

RECIPIENT PERIOPERATIVE PROTOCOL

IMMEDIATE PRE-OPERATIVE GOALS:

1. *PGE-1* by continuous infusion at 0.0125-0.05 mcg/kg/minute to maintain ductal patency, if indicated
2. Inotropic support and mechanical ventilation as indicated
3. Donor confirmation (with transport to Loma Linda or with distant procurement arrangements) signals additional recipient intervention by the surgical service. The recipient is to have two vascular lines placed in the left groin. One should be a central venous line and the other an arterial line. These may be positioned prior to transplantation or in the operating room
4. *Cyclosporine* continuous infusion at 0.1 mg/kg/hr per hour IV (D₅W-carrier) beginning as soon as donor is confirmed and consent for transplantation is signed (usually about six hours prior to transplantation). Discontinue at time of cardiac bypass and restart at the end of the procedure
5. To be given IV in the operating room:
 - a. *Cefazolin*:
 - 1) 20 mg/kg (birth to one month)
 - 2) 25 mg/kg (greater than one month)
 - b. *Methylprednisolone (Solumedrol)* 15 mg/kg
 - c. *Heparin* 3 mg/kg
6. All blood components for transfusion must have been screened for hepatitis, CMV, RPR, HIV and preformed donor-specific antibody, and have been irradiated before use and passed through a leukopore filter (see Blood Bank Protocol) If a patient is noted to have absent thymic tissue, blood needs to be sent to the Immunology Center for evaluation of DiGeorge Syndrome.
7. See Preoperative Order Form (Appendix)
8. For infants, the ICU Nursing Staff or Housekeeping should clean the infant warmer and add an eggcrate mattress with a clean baby blanket; cover bed with a clean sheet or blanket and have it sent to the operating room

IMMEDIATE POSTOPERATIVE GOALS:

1. Appropriate intravenous fluid replacement, respiratory and inotropic support
2. Uninterrupted hemodynamic monitoring during rewarming, transport, and in the ICU

Because of the age of these patients and their delicate hemodynamic balance, additional time may be required in the operating room at the end of the procedure to assure hemodynamic stability before transport to the ICU. During this time, the primary nurse from the ICU comes to the operating room to prepare the patient for transfer. This involves familiarizing her/himself with the invasive lines and drug regimen. He /she will initiate the surgeon's postoperative orders (e.g., fluid limits) and assess the general fluid balance state.

ANESTHESIA GUIDELINES

PREOPERATIVE MANAGEMENT

The skill with which anesthesia is administered to the recipient is important, as these infants have abnormal cardiorespiratory physiology. Management of this abnormal physiology may differ from that in the NICU or PICU because of the necessary changes in physiology which accompany the induction of an anesthetic state (intubation and mechanical ventilation) and the stress of operation prior to cardiopulmonary bypass (CPB). Deterioration in the physiologic state often begins during transport to the operating room. Infants whose inspired gas mixtures have been carefully controlled in the intensive care setting prior to surgery should generally be ventilated with nothing more than room air at a rate to maintain normal partial pressure of carbon dioxide. Hyperventilation with 100% oxygen will favor net pulmonary overcirculation, coronary artery “steal” and “unexplained” ventricular fibrillation among infants who have been previously stable for days and weeks.

Optimum management of the recipient requires communication at the attending physician level. When a decision to perform a transplant on an infant/child has been reached, the attending surgeon and attending neonatologist/pediatrician should confer with the attending anesthesiologist on call regarding the recipient's:

- a. Underlying anatomy
- b. Current physiologic status
- c. Venous access
- d. Type of monitoring catheters in place
- e. Need for ventilatory support/current respiratory status
- f. Current drug therapy
- g. Any additional complications or considerations

As time allows, the anesthesiology resident responsible for the case will make a preoperative assessment of the recipient:

1. Laboratory evaluation: Appropriate lab work will be available to the anesthesiologist including, but not limited to, CBC, electrolytes or random chemistry profile and ABG/CBG if indicated
2. Type and cross: Type and cross for protocol blood products will be accomplished prior to transport of the recipient to the operating room. Appropriate screening and labeling of blood products will be performed
3. Consent: Usually obtained by the surgeon. If time allows, discussion of the anesthetic care and risks with the recipient's parents/guardian and consent by them for anesthesia will be obtained by the anesthesiology resident involved with the case

OPERATIVE MANAGEMENT

In general, anesthetic care for transplant recipients will follow the current protocol for profound hypothermic circulatory arrest (PHCA). Some specific comments follow:

1. Operating room (O.R.) equipment set-up. The anesthesia aide/O.R. staff will assist by arranging the O.R. for pediatric cardiac surgery. Some specific equipment to be present in the O.R. includes:
 - a. Monitors
 - 1) EKG
 - 2) Non-invasive blood pressure (NIBP) (Dinamap or other)
 - 3) Pulse oximeter

ANESTHESIA GUIDELINES cont.

- 4) Stethoscopes: precordial and esophageal
 - 5) Temperature probes: esophageal, tympanic
 - 6) Capnometer
 - 7) Invasive monitors: arterial and central venous; with appropriate insertion kits
- b. Intravenous set-ups
- 1) Peripheral IV
 - 2) Blood warmer
 - 3) Manifold line/drug infusion line
 - 4) IVAC pumps for infusion lines
 - 5) Syringe pumps for drug infusions
 - 6) Selection of catheters for placing IV access

As per protocol for PHCA, all monitoring and IV infusion lines will be meticulously set up to prevent contamination or air embolus.

2. Medications

- a. Premedication, induction, and relaxant will be chosen by the attending anesthesiologist as deemed appropriate for the patient's physiology
- b. Preoperative infusions will be continued until recipient is placed on cardiopulmonary bypass (CPB) except:
 - 1) *PGE-1*--Patients who have been on *PGE-1* for prolonged periods may require slower weaning. A discussion regarding this will be carried out between anesthesiologists and surgeons prior to discontinuing *PGE-1* infusion
 - 2) *Cyclosporine*--Should be discontinued on CPB to preserve renal function
- c. Resuscitation drugs. These will be mixed by the anesthesiologist per protocol concentrations, and placed in syringes for use with syringe pumps. These will be present in O.R. prior to transport of the recipient to the O.R.
- d. *Methylprednisolone (Solumedrol)* -- 20 to 25 mg/kg IV is given at the beginning of anesthesia

Infusion drugs will be primed and in-line for immediate use as needed

Protocol concentrations of resuscitation drugs are important to decrease confusion on transport of the recipient to the ICU. The following concentrations of drugs will allow variation of drug amount per ml to permit constant infusion rates for certain common dosages:

<i>Dopamine</i>	1 ml/hr = 5 mcg/kg/min
<i>Dobutamine</i>	1 ml/hr = 5 mcg/kg/min
<i>Milrinone</i>	
<i>Amrinone</i>	1 ml/hr = 5 mcg/kg/min
<i>Nitroglycerin</i>	1 ml/hr = 1 mcg/kg/min
<i>Nitroprusside</i>	1 ml/hr = 0.5 mcg/kg/min
<i>Epinephrine</i>	1 ml/hr = 0.05 mcg/kg/min
<i>Norepinephrine</i>	1 ml/hr = 0.05 mcg/kg/min
<i>Isoproterenol</i>	1 ml/hr = 1 mg/kg/hr
<i>Tolazoline</i>	1 ml/hr = 1 mg/kg/hr

ANESTHESIA GUIDELINES cont.

Example: 2.1 kg recipient

Dopamine

1 ml/hr = 5 mcg/kg/min
= 10.5 mcg/min
= 630 mcg/hr

therefore, 630 mcg/ml concentration
therefore, 31.5 mg/50 ml syringe

Isuprel

1 ml/hr = 0.05 mcg/kg/min
= 0.1 mcg/min
= 6.3 mcg/hr

therefore, 6 mcg/ml concentration
therefore, 3 mg/50 ml syringe

The advantage of this system is that the controller setting for a given dose of a drug would be constant from patient to patient. This minimizes confusion regarding doses and controller settings from patient to patient. The disadvantage is the need to calculate a different concentration of each drug for each patient.

Under emergency conditions, at the discretion of the anesthesiologist, infusions will be mixed as deemed appropriate. Report will be given to the ICU staff to ensure continuity of infusions in equivalent concentrations.

PGE-1 (Prostin)--Prostin solution comes as 500 micrograms/ml. Standard concentration is 0.05 micrograms/kg/min, which is delivered at a minimum rate of 2-3 cc/hr. (syringe size=25cc)

To calculate this infusion, use the following:

Conversion factor is 0.05 multiplied by the patient's weight. This is equal to the number of cc's of *Prostin* to go into 25 cc D5/W. If this is run at 3 cc/hr, it is equal to 0.05 mcg/kg/min.

3. Airway management. Optimal oxygenation and ventilation parameters will be maintained as appropriate for the recipient's physiology prior to the time of CPB. Room air ventilation generally provides the best balance between systemic vs. pulmonary resistance. Postoperative ventilation will be continued through transport to the ICU. Extubation normally occurs in the ICU setting.

TRANSPORT MANAGEMENT

1. The operating room will notify the ICU when cardiopulmonary bypass is discontinued and the patient is ready for transport to the ICU. The primary receiving nurse will come to the operating room to help prepare the patient for transport. Report can then be given in a relatively stable setting prior to transport. Sufficient personnel to manage the equipment should be available from the surgical team to help transport the recipient to the ICU.
2. The recipient's crib / warmer will be in O.R., plugged in, and prewarmed. Sufficient battery powered syringe pumps will be used to continue infusions during transport. Battery powered monitors of EKG, arterial and central venous pressure and oxygen saturation will be used, in addition to any other monitoring equipment deemed appropriate. Oxygen and a pressure-monitored resuscitation bag will be used to continue controlled ventilation. Appropriate resuscitation drugs and fluids will be carried along on transport. The patient will be transported in an elevator carrying only the patient and personnel needed for transport.
3. The ICU will assume care of the patient once the patient is stable in ICU following transport.

OPERATIVE METHOD OF TRANSPLANTATION

Operative method of transplantation in neonates and young infants with cardiomyopathy is the same as for adults with the options of utilizing profound hypothermic low flow perfusion. Method of transplantation in neonates and young infants with hypoplastic left heart syndrome has been reported and is illustrated and summarized below.*

THE OPERATION (Figures 1-5)

A median sternotomy is utilized to perform thymectomy and expose the recipient's native heart. If the donor heart is significantly larger than the native heart, the entire left pericardium anterior to the phrenic nerve is removed. Single venous and arterial cannulation is generally employed. In infants with ductus-dependent systemic circulation, the ductus arteriosus is isolated and cannulated for arterial perfusion through a stab wound in the distal main pulmonary artery. All aortic arch vessels are isolated with loose tourniquets during the initial cooling phase in preparation for reconstruction.

More recently, the technique for transplantation that was previously described** has been modified. Implantation of the allograft is now accomplished with systemic hypothermia, performing the atrial anastomoses under low flow perfusion, with the pulmonary artery clamped and systemic perfusion maintained by means of the arterial cannula positioned in the ductus arteriosus. The aortic arch is then reconstructed under circulatory arrest with the arch vessel tourniquets tightened. The pulmonary artery anastomosis is completed while rewarming the patient.

Cardiectomy is performed in the standard fashion, leaving behind right and left atrial cuffs and the great vessels transected just above the semilunar valve commissural posts. The pulmonary artery is clamped. The donor graft is anastomosed to the recipient atrial cuff with a continuous polypropylene suture (6-0 or 7-0), starting at the lowest portion of the interatrial septum and proceeding to complete the right atrial anastomosis first. In older children, bi-caval anastomoses (as compared with atrio-atrial anastomoses) are accomplished, and in this setting, the left atrial anastomosis is completed first. Direct caval anastomoses are employed to minimize postoperative supraventricular tachyarrhythmias and augment atrial contractile performance. The graft is reflected towards the operating surgeon and the left atrial anastomosis is completed. Both chambers are filled with cold saline for air evacuation and myocardial preservation just prior to completion of the respective anastomoses. Using circulatory arrest, the ductus arteriosus is decannulated and ligated. Over 80% of neonates and infants require extensive aortic reconstruction. The undersurface of the recipient's hypoplastic aorta is opened and the anastomosis is directed from the descending aorta towards the aortic valve. The aortic cannula is then inserted in the innominate artery stump and cardiopulmonary bypass is reinstated. The pulmonary artery anastomosis is completed while the patient is being rewarmed.

Graft reperfusion and recipient rewarming are accomplished during 60-90 minutes of extracorporeal circulation. Median hypothermic circulatory arrest time has historically been 47 minutes at Loma Linda University. Circulatory arrest has not exceeded 20 minutes when utilizing the more recent modification outlined here.

Infusions of *dopamine* (2-3 mcg/kg/min), *tolazoline* (0.5-1 mg/kg/hr) and *isoproterenol* (0.01- 0.02 mcg/kg/min) are begun after approximately 30-40 minutes of graft reperfusion. Prostaglandin E1 infusion is continued initially, then weaned off over several days. Anticoagulation is reversed with protamine sulfate and hemostasis is achieved. Primary closure is performed in a standard fashion. Rarely, the incision is left open to avoid compression tamponade of the new graft. Delayed primary closure is accomplished after graft, mediastinal and chest wall edema has resolved. Post-operative ventilatory support is maintained for the first 24-48 hours among newborns and very ill young infant recipients. Older patients in the Loma Linda program who are stable prior to transplantation may be extubated in the operating room.

*Reference: Vricella LA, Bailey LL. Heart transplantation in children. In: Ginns LC, Cosini AB, Morris PJ eds. Transplantation. Cambridge: Blackwell Science ed, 1997: Chapter 16A (in press).

**Bailey LL, Concepcion W, Shattuck H, et al.: Method of heart transplantation for treatment of hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg* July 1986; 92(1):1-5.

REPLACE WITH FIGURES 1- 4 (COLOR INSERTS)

POSTOPERATIVE MANAGEMENT

GENERAL IN-PATIENT MANAGEMENT

The recipient is transferred from the operating room to a cardiac transplantation intensive care room. A 1:1 bedside nursing protocol is followed initially, using pediatric-trained personnel. A 1:1 respiratory therapist is also assigned to care for the infant/child. Routine post-cardiac surgical management is employed and may include mechanical ventilation and cardiac inotropic drugs. Standards of care are reflected in the post-operative order sheets and the clinical pathway (see appendix).

POSTTRANSPLANT TREATMENTS AND MEDICATIONS

1. *Cyclosporine (CSA; Neoral[®])*: Continuous IV infusion maintained at 0.1 - 0.2 mg/kg per hour (pending blood levels). When oral feedings are well tolerated, IV *cyclosporine* is discontinued and oral *cyclosporine* in a dose of approximately 10-20 mg/kg/day in divided doses every 8-12 hours is begun. A whole blood monoclonal antibody assay is employed to measure levels of *cyclosporine* on a daily basis until stable and then twice weekly. Target level is 250-300 nanograms per ml (whole blood) providing patient responds "normally." TID doses are generally required. A child less than four years of age should receive TID dosing because of more rapid CSA metabolism in younger children. Infants with impaired renal function may have decreased CSA target ranges if their rejection history is favorable. Some infants with absorption problems have been maintained on the intravenous preparation of *cyclosporine* given orally. (The IV preparation requires dose adjustment) (See appendix for potential drug interactions)
2. *Azathioprine (Imuran)*: 3 mg/kg/IV or orally once daily. Begun on first post-operative day. Dose is adjusted to keep WBC >4.0
3. *Methylprednisolone (Solumedrol)*: 20 to 25 mg/kg IV every 12 hours for a total of four doses given during the first two days after transplantation, then discontinued. Treatment of rejection is accomplished by giving *Methylprednisolone (Solumedrol)* 20-25 mg/kg IV every 12 hours for 8 doses
4. *Antithymocyte serum (ATS)*: Given as rescue therapy during episodes of acute rejection that are moderate to severe and/or unresponsive to steroids (0.5 mg/kg/dose IV for 7-10 days). ATS is generally used as prophylaxis for infants > 30 days of age (See Appendix)
5. *Antithymocyte globulin (ATGAM)*: Given as rescue therapy during episodes of acute rejection that are moderate to severe and/or unresponsive to steroids (15 mg/kg/day for 7-10 days) (See Appendix)
6. *Methotrexate*: Alternative rescue or maintenance therapy. Can be administered as a single dose or as three doses given every 12 hours once weekly or divided three times weekly (10 mg/m²/week). Keep WBC > 3000 (see Appendix)
7. *Tacrolimus (FK506/Prograf)*: Used for recalcitrant rejection. Induction drug level is 10-15 ng/ml for 3 weeks. Maintenance drug level is 8-10 ng/ml. FK506 should be administered at least one hour prior to, or 2 hours after eating
8. *Mycophenolate mofetil (CellCept)*. Used for recalcitrant rejection. Would replace *Azathioprine* or *Methotrexate*. Limited experience in young children. In older children and adolescents, begin at 250 mg po BID and gradually advance to a maximum dose of 2 gm per day. The capsules should be taken twice a day on an empty stomach. Patients are at an increased risk of developing lymphomas and other malignancies, particularly of the skin. The most common side effects are an increased susceptibility to infection, lymphoma, diarrhea, leukopenia, sepsis (generally CMV viremia) and vomiting. CellCept should be stored at room temperature.

POSTTRANSPLANT TREATMENTS AND MEDICATIONS cont.

9. *Rapamycin (Rapamune)*

Total Lymphoid Irradiation (T.L.I.): Reserved for severe chronic rejection unresponsive to other therapies. Total dose 800 rads. Do not withdraw other immunosuppression until effect of TLI is documented (See appendix)

10. *Intravenous immune globulin (IVIG, Sandoglobulin):* 400 mg/kg (12% solution) administered intravenously. This dose is repeated at least twice during the first week in the immediate postoperative period and may be repeated at times of increased immune suppression. A “mega” dose of 2 gm/kg (9% to 12%) may be used at times of severe rejection or prior to re-transplantation

11. *Ranitidine (Zantac):* 1 - 2 mg/kg/day divided every six to eight hours (IV dose); 2 - 4 mg/kg/day (15 mg/ml solution) divided every 12 hours (oral dose) (while taking *Solumedrol*)

12. *Cefazolin:* 20 mg/kg/dose IV every 12 hours (for infants from birth to one month of age); 25 mg/kg/dose IV every eight hours (for children greater than one month of age); continue until central lines are removed. Further antimicrobial therapy pending specific cultures

13. *Prostaglandin (PGE-1):* Initially at 0.05 micrograms/kg/min; weaned off over seven days following transplantation. Most commonly used for patients on PGE-1 prior to transplantation or for patients for whom pulmonary hypertension is anticipated

14. *Aspirin (ASA):* 3-5 mg/kg (1/2 baby ASA tablet for infants) per day is utilized when platelet counts are chronically > 500,000

15. *Ganciclovir:* 10 mg/kg/day divided every 12 hours for 14-21 days as specific treatment for CMV. Adjust dose downward for renal insufficiency; used in recipients who receive CMV positive grafts

16. *Acyclovir:* 30 mg/kg/day divided TID for 3 months after transplantation as prophylaxis against CMV (not necessary to use if Ganciclovir has been given)

17. *Anti-hypertensives* and suggested drug dosages:

a. *Propranolol*2 - 4 mg/kg/day po in 2 - 4 doses

b. *Hydralazine*0.75 - 3 mg/kg/day po in 2 - 4 doses

c. *Prazosin*.....0.05 mg/kg as test dose, then 0.25 mg - 1.5 mg/kg/day po in 4 doses

d. *Nifedipine*.....0.6 mg - 0.9 mg/kg/day po in 3 - 4 doses

e. *Metoprolol*.....1 - 5 mg/kg/day po in 2 doses

f. *Verapamil (25 mg/ml)*.....2 - 7 mg/kg/day po in 3 doses

g. *Minoxidil*.....0.2 - 1.0 mg/kg/day po in 1 - 2 doses

h. *Enalapril (Vasotec)*.....Starting dose = 0.1 - 0.5 mg/kg/day po in 1 - 2 doses (This increases serum K+)

POSTTRANSPLANT TREATMENTS AND MEDICATIONS cont.

- i. *Captopril*Infants 0.25 - 0.6 mg/kg/dose titrated upward to maximum of 4 mg/kg/day in 2 - 4 doses
.....Children 0.5 - 2 mg/kg/day every 8 - 12 hrs to maximum of 6 mg/kg/day.
.....Maximum dose 450 mg/24 hours.

- 18. Calcium channel blockers may be used as prophylaxis for posttransplant coronary artery disease or to improve renal perfusion: *Verapamil* 5 mg/kg/day divided TID for infants less than 6 months of age; *Diltiazem* 1 mg/kg/day given twice daily starting at 6 months of age. Cyclosporine dosage may need to be adjusted because of drug interactions.

CLINICAL SIGNS OF GRAFT REJECTION

1. Alterations in baseline cardiac rhythm
 - a. Increased resting heart rate
 - b. Arrhythmias, conduction changes
 - c. Bradycardia
 - d. Presence of third heart sound
 - e. Decreasing EKG voltage
2. Signs of poor contractility
 - a. Decreased function on echocardiogram. When the donor/recipient size mismatch is greater than 200%, the pediatric cardiologists may need to alter their echocardiographic interpretation of rejection due to “remodeling” effects. The infant may require the administration of a calcium channel blocker to relax the myocardium
 - b. Cool and mottled extremities
 - c. Rales
 - d. Hepatosplenomegaly
 - e. Oliguria
 - f. Diaphoresis
3. Congestive heart failure
 - a. Rales
 - b. Hepatosplenomegaly
 - c. Tachypnea
 - d. Advancing global cardiomegaly
 - e. Pulmonary edema and/or pleural effusion
4. Nonspecific
 - a. Irritability
 - b. Malaise
 - c. Change in feeding pattern
 - d. Change in sleeping pattern

Any recipient suspected of acute rejection should be treated using the rejection protocol. Histologic confirmation of rejection will be sought in cases of persistent or equivocal signs and symptoms.

REJECTION TREATMENT GUIDELINES

1. Asymptomatic/minimal symptoms:
 - a. Intravenous bolus steroid usually in outpatient setting (*Methylprednisolone (Solumedrol)* 20-25 mg/kg every 12 hours IV for eight doses in infants and *Methylprednisolone (Solumedrol)* 250-500 mg every 12 hours IV for eight doses in older children).
 - b. Ranitidine (*Zantac*) prophylaxis
 - c. Furosemide (*Lasix*) prn
 - d. May require transient treatment of hypertension
2. Moderate-severe symptoms:
 - a. Inpatient intravenous bolus steroid (as above), and/or
 - b. *Thymoglobulin* (equine) 1.5 mg/kg/day IV for 7 days in the intensive care setting
 - c. *Antithymocyte serum (rabbit)* 0.5 cc./kg/day IV for 7- 0 days in intensive care setting (see Appendix)
 - d. *Antithymocyte (ATGAM) (equine)* 15 mg/kg/day IV for 7-10 days in intensive care setting (1 mg/1cc in D5/.45) (see Appendix)
 - e. *Methotrexate* - 10 mg/m²/week; once a week
 - f. Extracorporeal membrane oxygenator (ECMO): optional rescue therapy
 - g. Consider conversion to Tacrolimus (*FK506, Prograf*)
 - h. *OKT-3*
 - 1) Rarely used in young children
 - 2) 3-5 mg intravenously. Administer as a bolus for 5-10 days. Infuse over 10 minutes
 - 3) Intravenous or oral steroid administration should continue on course
 - 4) *Benadryl* 1 mg/kg/intravenously given slowly before OKT-3 infusion begun
 - 5) *Tylenol* elixir or suppository (for age)
3. *Ranitidine (Zantac)*
 - a. Intravenous dose: 1-2 mg/kg/day in divided doses every six to eight hours
 - b. Oral dose: 2-4 mg/kg/day divided every 12 hours
4. Furosemide (*Lasix*): as necessary
5. Emergency kit in case of anaphylaxis
 - a. Two vials *Methylprednisolone (Solumedrol)* (125 mg)
 - b. Three vials *Epinephrine* (1:10,000)
 - c. Three vials *Benadryl* (50 mg)

DISCHARGE MEDICATIONS

Cyclosporine (Neoral) 10-20 mg/kg/day, orally, in divided doses every 8-12 hours depending on blood levels
Azathioprine Emulsion (Imuran) (10 mg/cc) 3 mg/kg/day, orally, once daily (see Appendix for preparation)

The following medications are taken during the first three months after transplantation:

Poly-vi-sol

Acyclovir

Fer-in-sol

Nystatin

MANAGEMENT OF LONG-TERM IMMUNOSUPPRESSION (ASSUMING FAVORABLE REJECTION HISTORY)

1. *Cyclosporine*(*Neoral*®). Lower target trough *cyclosporine* levels to 150-200 ng/ml after three months posttransplant (Cobas-Emit whole blood, monoclonal antibody, measuring parent compound) if rejection history has been favorable. Lower target range to 100-150 ng/ml after one year if rejection course continues to be benign. Assure adequate CSA levels during times of presumed rejection
2. *Azathioprine* (*Imuran*). Initial postoperative dose is 3 mg/kg/day as tolerated (keep WBC>4.0). In rare cases at one year posttransplant, the drug may be discontinued if infant was less than 30 days of age at time of transplant. For infants older than 30 days, *Imuran* will be continued indefinitely at a dose of 1 mg/kg/day, (keeping WBC > 4.0). Continue *Imuran* in any patient with a history of multiple rejection episodes
3. Immunosuppression will be maintained at higher levels for those who have had a difficult rejection course and may include long-term *Methotrexate* in place of *Imuran*. Late rejection episodes create a high index of suspicion and a concern about the potential development of posttransplant coronary artery disease

OUTPATIENT FOLLOW-UP: FREQUENCY OF VISITS

Following discharge, recipients initially return to the transplant clinic of the International Heart Institute for outpatient evaluation twice weekly, then weekly and monthly for the first year. Principal follow-up physicians are from the Department of Pediatrics. Outpatient visits are organized by the cardiac transplant coordinators who are in attendance during each outpatient visit. EKG voltage is measured and plotted on a graph. Data collection is the responsibility of the transplant coordinators and follow-up physicians. All data are to be reviewed within 24 hours of each outpatient visit.

Telephone calls from recipient families are to be directed to the "on call" cardiac transplant coordinator, who will triage information to the follow-up physician.

If significant rejection or infection are suspected, outpatient visits become more frequent, and the patient may be hospitalized. The recipient will be hospitalized into an intensive care (1:1) setting if rejection is suspected and/or the rejection episode is responding poorly to outpatient administration of steroids. Responsibility for care is shared between the Cardiac Surgery Service and Transplant Pediatrics.

LONG-TERM FOLLOW UP GUIDELINES

Routine follow-up to be done at three month intervals, usually at outlying facility.

A lifetime commitment to follow-up is presumed to be mutually beneficial to both recipient and transplant center.

INFORMATION MANAGEMENT

The Cardiac Transplant Team is currently using a SQL relational database which runs on a local area network (LAN) using Windows based interface. The database and the data entry interface were developed at Loma Linda. There are over one hundred data fields which are available. All components of the evaluation, transplant and follow-up functions of the team can be entered in real time. In addition, data retrieval is easily accomplished via several commercially available reporting tools. Electronic mail is available for use by the transplant team in communicating locally, within the university and around the world over Internet.

RECOMMENDED OUTPATIENT TESTING SCHEDULE

TEST	FREQUENCY
1. Routine physician visit	Twice weekly for 6 weeks post hospital discharge, then less frequently as rejection-free interval widens. Minimum frequency interval is every month for first posttransplant year, then every three months thereafter
2. Echocardiogram/EKG	Three times per week for 2 weeks (in-hospital) then twice weekly for 4 weeks, then less often as rejection-free interval widens. Once a month for the first posttransplant year and every three months thereafter
3. “Full study” echocardiogram to evaluate aortic arch	1 month, 3 months and 12 months posttransplantation
4. Cardiology clinic visit	3 months and 12 months posttransplantation and as indicated
5. Chest x-ray	Once a week for 2 weeks post hospital discharge, then monthly for 3 months; at 6 and 12 months and annually thereafter
6. Cyclosporine level (trough)	Twice a week for 2 weeks post discharge, then weekly for 4 weeks. Monthly for the first year and every three months thereafter
7. CBC and platelets	Every 2 weeks for 2 months and monthly for the first year posttransplantation. Every 3 months thereafter
8. Basic electrolytes	Weekly for 2 weeks, then every 2 weeks for 2 months posttransplantation, then monthly for one year posttransplantation. Random chemistry panel (to replace basic lytes) monthly during first year, then every 3 months thereafter
9. CMV IgG titer	6 months and 12 months posttransplantation and every year thereafter
10. HIV, Hepatitis B Surface Antigen	6 months posttransplantation
11. EBV (IgG and IgM) titers	6 months posttransplantation (held in Cardiac Serum Bank - to be run at a later time, if needed)
12. Occupational therapy	Developmental assessment at 4 months and 18 months of age
13. Language and speech evaluation	3 years of age for those transplanted in infancy (to be arranged through local school district)

RECOMMENDED OUTPATIENT TESTING SCHEDULE cont.

14. Standard psychometric testing	5 years of age for those who were transplanted in infancy
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- | | |
|---|---|
| 15. Isotopic glomerular filtration rate | 3 months and 12 months posttransplantation and every year thereafter (every 2 years if older than one year of age at time of transplant) |
| 16. Renal ultrasound | 3 months, 12 months and 36 months posttransplantation and every <u>other</u> year thereafter for those transplanted at less than one year of age; frequency is every other year for those transplanted at greater than one year of age. |
| 17. Metabolic exercise stress test | For infant recipients, test at 6 years of age and annually thereafter. For those children greater than 6 years of age at time of transplant, test at 6 months posttransplantation and annually thereafter |
| 18. Dobutamine stress echocardiography | Annually, beginning at 3 years posttransplantation if < 2 years of age at time of transplant. If > 2 years of age at time of transplant, check DSE at 2 years posttransplantation and annually thereafter. |
| 19. Biopsy | |
| Newborn - 2 years at time of transplant | Annually |
| 2 - 8 years of age at time of transplant | 1 month, 3 months and 12 months posttransplantation and annually thereafter |
| 9 years and older at time of transplant | 1 month, 2 months, 3 months, 6 months, 12 months posttransplantation and annually thereafter |
| Post re-transplantation | 1 month, 2 months, 3 months, 6 months, 12 months posttransplantation and annually thereafter. |
| 20. Heart catheterization; coronary angiogram; “full study” echocardiogram | Annually |

ROUTINE PEDIATRIC CARE

Formula and diet - as per usual for normal well infant

Immunizations - usual schedule for polio (using killed virus) and DPT/Hepatitis B/Hib beginning between third and fourth postoperative month (see infectious diseases guidelines). MMR and chickenpox vaccines deferred. Pneumovax at 24 months. Annual influenza vaccination. Should be six weeks post immune globulin before receiving vaccinations. Do not attempt to taper immunosuppression while immunizing

Circumcision - may be performed in the NICU at parent's request with three-day antibiotic prophylaxis

Exposure to sunlight - exposure to sunlight is an important factor in the development of skin cancer; patients should avoid excessive exposure, particularly those who are at high risk for skin cancer: light skinned individuals, with blue eyes and blond or red hair. Alternatively, skin should be protected by regular use of sunscreens, containing agents such as para-aminobenzoic acid, which filter out the harmful ultraviolet-B rays

OUTPATIENT INFECTIOUS DISEASES GUIDELINES

1. Cytomegalovirus and other herpes group of viruses surveillance and management:
 - a. CMV titers (IgG) 6 months posttransplant, then yearly, using 3 pooled urine specimens for viral evaluation
 - b. Intravenous immune globulin (*IVIG*, *Sandoglobulin*) is used posttransplant for passive immune enhancement. May also be administered during times of increased immune suppression at a dose of 400 mg/kg/dose (12% solution). "Mega" doses of *IVIG* (2gm/kg) may be used in certain circumstances (severe rejection; re-transplantation)
 - c. When CMV infection is confirmed (four-fold increase in titer, positive urine and/or throat cultures), *IVIG* will be administered at 400 mg/kg/dose at regular intervals and *Gancyclovir* 5-10 mg/kg/day will be administered for 14-21 days
Liver function tests, blood gases (if indicated), and chest x-ray will be performed at the time of CMV diagnosis. Fundoscopic examination by an ophthalmologist may be done at the time of CMV diagnosis to assess chorioretinitis
 - d. EBV (IgG and IgM) titers are tested pre-transplant; annual specimens are collected and stored for future use
 - e. It has been observed that respiratory syncytial virus (RSV) and other viruses (e.g. adenovirus) may stimulate a rejection response. Stepped-up surveillance for rejection should accompany these diagnoses
 - f. PCR evaluation as indicated

2. Immunizations:
 - a. DPT (diphtheria, pertussis, tetanus), polio-virus (Salk inactivated vaccines) Hepatitis B/Hib will be given at usual age of childhood immunizations (2, 4, 6, 18 months and 5 years of age) unless contraindicated.
Contraindications include acute febrile illness, acute rejection episodes, seizures (for pertussis component), adverse reactions, or recent immune globulin therapy (should be 6 weeks post-*IVIG*). Do not attempt to taper immunosuppression when immunizing
 - b. MMR (measles, mumps, rubella) and chickenpox vaccines to be deferred until further information indicates otherwise
 - c. Hemophilus influenza (Hib) will be administered at same time as DPT and polio; pneumococcal vaccine (pneumovax) will be administered at 24 months of age
 - d. Yearly influenza vaccine beginning at 6 months of age

OUTPATIENT INFECTIOUS DISEASES GUIDELINES cont.

- e. Exposure to MMR: prophylactic ISG (immune serum globulin). Exposure to chickenpox: VZIG for the following conditions:
 - 1. Less than one year posttransplant
 - 2. Currently taking either *Prednisone* or *Methotrexate*

We believe it is only necessary to administer prophylaxis against chickenpox when an additional compromising factor is present. Ultimately, it will probably be safer for children to experience chickenpox rather than to wait for adulthood when secondary complications are prevalent. *Acyclovir* is administered for active chickenpox lesions at a dose of 80 mg/kg, divided every 8 hours for 7 days.

- f. TB skin test at one year

3. Intercurrent Infections

All intercurrent infections will be evaluated as soon as possible and managed by the primary physician. Attempts toward documentation of the etiologic agent and of the state of the immune response should be performed inasmuch as the patient's condition allows.

DENTAL CARE GUIDELINES

Routine pediatric dental care should begin around two years of age

All dental procedures likely to induce gingival bleeding (not simple adjustment of orthodontic appliances or shedding of deciduous teeth) should be preceded by prophylaxis for endocarditis

PROPHYLACTIC REGIMENS:

Standard: *Penicillin V* 2 grams orally one hour before, then 1 gram six hours later; for patients unable to take oral medications: 2 million U of aqueous *penicillin G*, IV or IM, 30-60 minutes before a procedure and 1 million U six hours later, may be substituted

Special: Parenteral regimen for use when maximal protection desired. *Ampicillin*, 1-2 grams IM or IV, plus *Gentamycin*, 1.5 mg/kg, IM or IV, one-half hour before procedure, followed by 1 gram oral *Penicillin V* six hours later; alternatively, parenteral regimen may be repeated once eight hours later.

Gingival hyperplasia may be minimized by rinsing the child's mouth immediately after dosing with CSA.

GUIDELINES FOR INVASIVE FOLLOW-UP STUDIES

For infants who undergo transplantation, endomyocardial biopsies are not done routinely during the first year posttransplant. At or near the end of the first posttransplant year, the infant will undergo a complete heart catheterization and endomyocardial biopsy, including aortic root injection and selective coronary catheterization for coronary arteriography. Also included will be:

- 1. 2-D-Doppler and M-mode echocardiogram
- 2. 12-lead electrocardiogram
- 3. Dobutamine stress echocardiography

INDICATIONS FOR RETRANSPLANTATION

Irreversible graft dysfunction or life threatening events associated with severe graft vasculopathy, in cases where irreversible damage to other organs has not occurred and there exists a reasonable chance for a good long-term outcome. It is understood that there will be the need for more aggressive immunosuppression for patients who undergo retransplantation.

PROTOCOL FOR PEDIATRIC HEART TRANSPLANTATION AUTOPSIES

Since each transplant recipient's course is different, the death of each patient presents a unique opportunity to learn more about the effects and side-effects of transplantation in these young children. It is therefore very important that a thorough autopsy be performed whenever a death occurs. The aim of the autopsy should be not only to establish the cause of death as accurately as is possible, but also to evaluate the effects of current forms of therapy in this age group, and to detect and delineate any intercurrent processes, both known and unsuspected.

The families of the pediatric heart transplant recipients are strongly encouraged to consent to an autopsy in the event of the recipient's death. Most families readily agree when they understand the important contribution their child can make on behalf of other children in furthering our understanding of transplantation. This is, of course, a delicate subject, but must be approached in a timely manner in order not to unduly delay the commencement of the autopsy, particularly when infection is suspected. The pathologist should be notified directly by a member of the transplant team in a timely fashion when one of the transplant patients dies and consent for autopsy has been obtained or is anticipated. We have found the following guidelines useful:

1. It is critical that the transplant surgeon, transplant coordinator and/or other senior member of the transplant team communicate directly with the pathologist responsible for the autopsy in a timely fashion, relaying relevant clinical information regarding the clinical course of the patient and suspected problems, both short-term and long-term. If the pathologist has not been contacted by the transplant team, it is his or her responsibility to contact them before commencing the autopsy. Without an informed approach to the autopsy, relevant findings may be overlooked, even by an experienced pathologist. Important information might include, but not be limited to, the following:
 - a. Age of the patient, and age of donor
 - b. Any unusual aspects of the donor heart procurement or transplantation, e.g. prolonged graft ischemic time, unusually large heart
 - c. Reason for transplantation, e.g., cardiomyopathy, AV canal (with or without pulmonary hypertension), severe endocarditis, etc.
 - d. Length of time the transplanted heart has been in place
 - e. Significant diseases or problems documented or suspected prior to death, occurring either before or after transplantation, including any rejection history
 - f. Mode and clinical suspicion as to cause of death
 - g. Details of culture results, pending cultures, and specific antimicrobial therapies employed, if infection is suspected
2. Photographs of major lesions or other interesting findings should be taken during or immediately after the dissection. These are useful for documentation as well as teaching during later review of the case with the transplant team.
3. Transplant patients have an increased susceptibility to infection. Therefore, the blood and lung should be routinely cultured for bacterial, fungal and acid fast organisms. (In cases where the autopsy examination has been delayed for several days after death, one may elect not to perform the routine bacterial cultures.) Additional cultures should be taken from sites that were clinically suspected to be infected, or lesions deemed suspicious at the time of autopsy. When the suspicion of infection is high, consideration should be given to obtaining blood cultures immediately following death (by members of the transplant team), before the body is transferred to the morgue.
4. Viral cultures are not routinely obtained. However, when viral infection is a clinical consideration or suspicion, fresh sections of liver, kidney and lung, together with samples of blood and urine, should be sent for viral culture. These studies should be coordinated with the virology laboratory, so that the specimens are appropriately collected and promptly processed.

PROTOCOL FOR PEDIATRIC HEART TRANSPLANTATION AUTOPSIES cont.

5. While conventional autopsy technique will be satisfactory in most instances, the dissection should be modified to address the concerns of each case as necessary. All organ systems should be thoroughly examined and sampled. A few special considerations are outlined below:
 - a. **Heart**—Typically the heart is fixed whole after removal following preliminary examination and harvesting of tissue for snap-freezing and any other special studies. It is then examined in detail and sectioned after fixation. If the autopsy is performed at an institution with limited experience in cardiac transplantation, one may wish to ship the heart to a center more experienced with cardiac transplant pathology. At a minimum, sections of the heart should include right ventricle and left ventricle (with papillary muscles), interventricular septum and all three major coronary arteries. The coronary arteries should be examined in particular detail in patients more than 12 months posttransplant. Anastomotic lines should be examined for dehiscence, stricture or coarctation. If possible, any structural abnormalities should be reviewed with the transplant surgeon while the heart is fresh.
 - b. **Lungs**—The lungs are the most common source of infection in transplant recipients. After securing appropriate cultures and snap-frozen tissue, one lung should be fixed by bronchial infusion of 10 % formaldehyde (or similar fixative) for 24 hours at room temperature before further cutting.
 - c. **Hematopoietic/lymphoid**—Particular attention should be paid to the bone marrow, spleen, and lymph nodes for evaluation of the degree of immunosuppression, of possible opportunistic infection, and possible emergence of malignancy, primarily in the form of a posttransplantation lymphoproliferative disorder (PTLD). The latter can develop within a relatively short period of time following transplantation (as early as a few months), and if significant adenopathy is present, or if a PTLN is otherwise suspected, portions of lymph node (or other relevant tissue) should be snap-frozen as well as portions fixed in B-5 or similar fixative for optimal evaluation of lymphoid morphology.
 - d. **Brain**—If consent for autopsy includes evaluation of the brain, the brain (and spinal cord, if desired) should be taken and fixed for neuropathologic study. Hypoplasia or reduced myelination of the white matter is a fairly common finding, and the brain may also be the site of opportunistic infection, infarction or lymphoma. Herpes virus may be found in dorsal root ganglia of the spinal cord.
6. Blocks of fresh, unfixed myocardium, liver, kidney and lung tissue should be snap-frozen and stored at -70° C in anticipation of possible future studies requiring frozen tissue (such as PCR for specific micro-organisms or molecular studies for lymphoproliferative disorders).
7. If desired, samples of heart, kidney, liver (and/or other organs as deemed appropriate in view of the clinical history) can be fixed in glutaraldehyde for electron microscopy. Suspected herpetic or other viral lesions would be an example of indications to reserve tissue for electron microscopy.
8. To maximize the learning potential of the autopsy, major or unsuspected lesions should be discussed and/or demonstrated to the appropriate clinical attending physician(s) in the fresh state, at the time the autopsy is performed, whenever possible.

APPENDIXES

ADMINISTRATIVE COMMITMENT

The heart transplantation program at Loma Linda University Medical Center represents a wide and deep commitment both in our past and to our future. We are committed to provide transplantation therapy to carefully selected adults and children with fatal heart defects or disease. We are also committed to a vigorous program of research in a broad range of issues--medical, social, and ethical--surrounding heart transplantation. We are committed to sharing our findings through publications, presentations, and on-site visits and training for the professional community.

A strong interdisciplinary team has emerged, actively dedicated to the success of heart transplantation. Loma Linda University Medical Center regularly serves as host to numerous transplant physicians and nurses who study this program as a model for their own institutions. In March, 1990, the transplant team sponsored the first Loma Linda International Conference on Pediatric Heart Transplantation, drawing 500 transplant professionals together to share their experience. Subsequent conferences have been equally successful. Loma Linda plays a prominent role in national and international professional meetings and is an integral part of an international network of transplant professionals. The imagination of researchers and clinicians at LLUMC has been stimulated by this diverse group of individuals who are committed to improving the quality of life for these children and adults. Loma Linda University Medical Center clinicians recognize and accept the responsibility for world leadership in this field.

Nurturing of the heart transplant program at Loma Linda has involved a significant institutional financial commitment. In addition to expenses of clinical care absorbed by the Medical Center, Loma Linda faculty physicians, largely from the Department of Surgery, have contributed over \$5.2 million to research in transplantation since 1983.

The Cardiac Transplant Center is housed in prime office and clinical space on the lobby-level of the Medical Center's Schuman Pavilion in an area called the International Heart Institute. The nurse coordinator staff for the transplant program has 5.0 FTE's. They are supported by 1.5 FTE's who function as clinic nurses, 3.0 FTE's who function as secretarial support, 1.0 FTE data management support and 1.0 FTE who serves the social work needs of transplant recipients and their families. These personnel are funded by Loma Linda University Medical Center.

Physician support for follow-up is provided by general pediatricians with subspecialty support available as needed.

Key to the heart transplant program's success are the team members who meet on a weekly basis to discuss patient care issues. The weekly pediatric patient care committee is chaired by the Medical Director. At these meetings, team members share the results of recent laboratory tests and clinical examinations of the transplant patients. Policies are reviewed and revised to maintain current protocols. Potential recipients are discussed and evaluated. This meeting also provides a forum for morbidity and mortality reviews, evaluating research protocols and results, and other quality improvement projects.

PRE-TRANSPLANT EVALUATION CHECK LIST

- REQUIRED:
- Medical records/birth history
 - Weight, head circumference, length (at birth)
 - Videotape of echocardiogram
 - Heart catheterization report/cine angiogram (if done)
 - Neurologic assessment (may include head ultrasound/MRI/CT)
 - EEG
 - Head CT
 - Head US
 - MRI
 - Confirmation of blood type
 - CBC with differential, platelet count
 - Basic electrolytes
 - CMV titer (IgG)
 - RPR (or equivalent)
 - Hepatitis B surface Ag
 - HIV
 - PRA (percent reactive antibody)
 - 1.0 cc in red top tube at room temperature
 - Send to LLUMC
 - Urine for culture
 - Blood for culture
 - E.T.T. aspirate or nasopharyngeal swab for culture
 - GFR (Glomerular Filtration Rate)
 - Renal ultrasound
 - Chest x-ray with KUB
- AT TIME OF TRANSPLANT:
- EBV-IgG, IgM
 - HLA typing

CARDIAC TRANSPLANTATION EVALUATION WORKSHEET

**INTAKE INFORMATION FOR POTENTIAL
HEART TRANSPLANT RECIPIENT
(FETUS)**

Interview Date: _____

EDC _____ Gest. Age _____

Patient's Name _____ Mat. DOB _____

Patient File #: _____

Referring Physician _____

Maternal Age _____ G _____ P _____ Bld Type _____ EDC _____

History of blood products or atypical Ab _____

Maternal Health Problems: _____

Patient Blood Type _____

How was diagnosis made?

Results of high resolution fetal ultrasound looking for other anomalies:

Chromosomal analysis by amnio?
Results:

Chorionic villus sampling?

Other pregnancy complications?

Anticipated mode of delivery.

**INTAKE INFORMATION FOR POTENTIAL
HEART TRANSPLANT RECIPIENT
(NEONATE)**

Please list known transfusions of any blood products dates. Please include quantity if known.

Type	Date	Quantity
------	------	----------

Neurologic Evaluation:

Tone?

Moro? _____ root? _____ suck? _____

gag? _____ fencers? _____

Ultrasound?

CT or MRI studies?

Seizures?

Phenobarbital?

Why?

Other anticonvulsants?

Patient Name _____ DOB _____

**INTAKE INFORMATION FOR POTENTIAL
HEART TRANSPLANT RECIPIENT
(CHILD)**

Interview date: _____

Pediatrician: _____

Name:

Date of Birth:

Address:

Referring Physician(s) and address(es):

History of Cardiac Disease:

Has patient been evaluated by any other specialty (i.e., neurology, genetics, infectious disease, etc.)? If so, please give dates and impressions.

Past Medical History

Birth: Mother's Age _____ Gravida _____ Para _____ Ab _____

Pregnancy Complications:

Delivery Type: (Check all that apply)

_____ Vaginal _____ Cesarean _____ Forceps _____ Breech

Delivery Complications:

Estimated Gestational Age at delivery _____ weeks

Apgars _____ 1 minute _____ 5 minutes

Postpartum complications:

**INTAKE INFORMATION FOR POTENTIAL
HEART TRANSPLANT RECIPIENT
(CHILD)**

Feeding: Did patient have any feeding difficulties or allergies?

What is patient's current diet?

Development: Age at which patient achieved the following milestones:

smiles _____

grasped objects _____

sat _____

crawled _____

walked _____

ate with utensil _____

spoke words _____

spoke sentences _____

potty trained-day _____

potty trained-night _____

rode tricycle _____

If patient is in school, please complete the following:

Grade _____

What type of grades is the patient currently making?

Is there any history of learning problems in school?

Is there any history of significant behavior problems?

Medical/Surgical:

Does patient have any additional medical problems?

Previous surgeries?

Any known allergies?

Current medications and dosages?

Patient Name _____

**INTAKE INFORMATION FOR POTENTIAL
HEART TRANSPLANT RECIPIENT
(CHILD)**

Family history:

Please list any inheritable or chronic conditions in family members

Review of Systems:

Please complete the following questions as applicable:

Renal: Is there any evidence of dysfunction? Yes No
Creatinine highest _____ current _____
BUN highest _____ current _____
Potassium highest _____ current _____

Liver: Is there any evidence of dysfunction? Yes No
Liver function studies - highest with dates

Liver function - current

Gastroenterology: Is there any evidence of dysfunction? Yes No

Infectious Disease/Immunology: Is there any evidence of active or recent infection? Yes No

Results of most recent blood C & S: Date:

Results of most recent urine C & S: Date:

Results of most recent other C & S: Date:

Results of most recent CBC: Date:

Have there been any positive cultures in past?

Results of:

RPR Date: HepBsAg Date:

HIV Date: CMV Date:

Patient Name _____

SOCIAL SERVICE EXPERTISE AND COMMITMENT

Services:

Social work services are provided for heart transplant recipients and their families to help them address emotional and social issues which interfere or adversely affect medical treatment or compliance with the medical regimen. Social workers contribute to treatment efficacy by enhancing the patient's ability to cope with the therapy process.

Services available to heart transplant patients are:

Case management	Resource acquisition
Psychosocial evaluation	Community referral
Crisis intervention	Discharge planning
Counseling	

Social work involvement with typical heart transplant families begins shortly after the patient, family, or referring physician has made an initial inquiry relative to patient suitability for treatment. The social worker collects background information from the social worker at the referring hospital. This information is incorporated into the initial psychosocial evaluation.

The initial contact between the patient or family and the social worker often takes place over the phone. It is during these early contacts that the social worker seeks to enhance the patient's and/or family's understanding of the treatment and recovery process, gather information for the psychosocial evaluation, and work out any logistical considerations such as transportation, housing and finances.

Many families stay, for a time, at one of the two homes provided by the Medical Center. These serve as transitional living quarters until the social worker can assist the family in securing more permanent housing in the community. More recently, a Ronald McDonald house has opened to accommodate families of hospitalized children.

Upon acceptance into the program, the social worker's role becomes one of general case management, facilitator, and counselor. The social worker helps the patient and family cope with treatment, locate needed resources and make transitional and adjustment arrangements. Social work support and involvement continue throughout hospitalization. Post-hospitalization, social work staff periodically review the patient's circumstances and provide services as needed. The social worker acts as a resource person for the Patient/Family Support Groups.

FINANCES

Patients accepted into the Loma Linda University Medical Center Heart Transplant Program must have financial resources available to pay for transplantation. Sufficient insurance coverage and authorization for transplant must be verified prior to listing the patient as a potential recipient for an available organ.

If sufficient insurance reimbursement is not available, private arrangements must be made with the LLUMC Patient Business Office in advance. Sufficient resources for outpatient follow-up care and pharmaceuticals must be available and confirmed prior to surgery.

The patient/family will be responsible for providing resources for living expenses, including transportation to and from the heart transplant clinic during the pretransplant period and the posttransplant follow-up period. The patient must reside temporarily within a 45-60 minute travel time to LLUMC for up to six months post transplantation.

**INFORMED CONSENT FOR RECIPIENT REGISTRATION
FOR HEART TRANSPLANTATION**

I have met with Dr. _____ regarding my child's candidacy for heart transplantation at LLUMC. My child's heart problem has been explained to me by a pediatrician or cardiologist, and I understand that it is serious enough for us to consider heart transplantation. I have had my questions answered about my child's heart problem.

I have had an opportunity to review the videotape explaining the risks of heart transplantation and I have discussed these risks with Dr. _____. I understand these risks to include:

1. The risks of open heart surgery, including the risk of death, brain damage, or other organ damage such as kidney injury.
2. The need for blood transfusion during surgery with the risk of infection from the blood or a reaction to the blood.
3. The risks of damage to the new heart by my infant's body rejecting the new heart.
4. The risks of immune suppression medications required to prevent rejection of the new heart including:
 - a. An increased risk of infections.
 - b. An increased risk of blockage of the coronary arteries.
 - c. Perhaps an increased risk of cancer or tumors after several years of these medicines.
 - d. Potential kidney toxicity such as high blood pressure or loss of salts in the urine.
5. There may also be additional risks that are as yet unknown to us.

I understand that by signing this form I am requesting that my child be registered for heart transplantation. I also understand that I can change my mind at any time up until the time of surgery. I understand that my child's status may change so that he is no longer a candidate, and I will be informed of this should it occur. I understand that I will need to sign an additional consent form at the time of surgery. I accept that if my family lives more than 30-40 minutes traveling time from LLUMC, relocation closer to the medical center may be required. I also commit to the required follow-up schedule. Inherent in my consent for surgery will be my approval for a postmortem examination (autopsy) in the event of my child's death at any time after transplantation. Furthermore, I understand that my consent for transplantation may involve participation in diagnostic studies that endeavor to improve the quality of life for these transplant recipients.

Signature of Child (required if over 7 years old)

Signature of Mother

Date

Witness

Date

**INFORMED CONSENT FOR RECIPIENT REGISTRATION
FOR HEART TRANSPLANTATION**

Signature of Father

Date

Signature of Legal Guardian

Date

CARDIAC DONOR CHECKLIST

**NEONATAL/PEDIATRIC PRE-CARDIAC
PHYSICIAN ORDER SHEET**

OPERATIVE NOTE: ORGAN PROCUREMENT/DONOR

NAME:

DATE OF BIRTH:

HOSPITAL CHART NUMBER:

DATE OF OPERATION:

PRE-OPERATIVE DIAGNOSIS: Brain Death

POST-OPERATIVE DIAGNOSIS: Brain Death

OPERATION: Median Sternotomy, Donor Heart Procurement

SURGEON(S):

DESCRIPTION OF PROCEDURE: After placement in the supine position, the chest and abdomen were prepped and draped in the usual sterile fashion. The standard median sternotomy was performed. The thymus was excised and removed for lymphocyte testing. The innominate vein was identified and divided between silk ties. The great vessels were then divided between liga clips. The ascending and transverse aorta were completely dissected free with extension down past the ductus arteriosus on the descending aorta. After freeing up the aorta, the pericardium was incised with excision extended into both chest cavities inferiorly. The heart was noted to be beating vigorously. The superior vena cava was looped with a heavy tie just below the take off of the azygos vein. The descending aorta was similarly looped with a heavy tie just below the take off of the azygos vein. The descending aorta was similarly looped with a heavy tie below the ductus. A 7-0 prolene purse string suture was placed on the ascending aorta and a cardioplegic needle was inserted in the ascending aorta and 20 cc of blood was removed for lymphocyte testing.

A cross-clamp was placed on the descending aorta and cold crystalloid cardioplegia was infused into the aortic root. The heart was lifted superiorly and the pulmonary veins were cut at their entrance to the left atrium. The superior vena cava was tied superiorly and then cut just below the tie. The pulmonary artery was then cut at the bifurcation of the left and right pulmonary arteries and the aorta was excised after tying the descending aortic tie. The donor heart was then removed to an iced saline bath, where it was trimmed appropriately. Five lymph nodes were taken from the mesentery of the colon and a wedge biopsy of the spleen was taken for lymphoid examination. Following excision, the chest was closed in standard fashion.

OPERATIVE NOTE: Organ Procurement/Donor
LOMA LINDA UNIVERSITY MEDICAL CENTER

CARDIAC TRANSPLANT NURSE COORDINATOR OPERATING ROOM PROTOCOL

OBJECTIVE:

To provide a controlled, organized, safe environment in which to accomplish cardiac transplantation.

IMPORTANT POINTS:

1. Because of immunosuppression, the cardiac transplant candidate has an increased susceptibility to infection.
 2. Persons not actively involved in the transplant should be limited. The circulating nurse is authorized to maintain control of personnel and traffic in the operating room.
-

METHOD	KEY POINTS
1. Receive notification of the following: a. Name, age and identification number of recipient b. Location of the recipient c. Time of surgery d. Name of surgeon and assistants	Cardiac Transplant Coordinator or surgeon will notify the O.R. nurse in charge, carrying beeper 4531.
2. Contact personnel one hour before time of surgery	a) Cardiac nurses b) Perfusionist c) Blood Gas Technician d) Anesthesia Technician on call
3. Prepare instruments, drapes and supplies for cardiac surgery	Use Doctor's Preference Card
4. Receive patient into operating room	

**CARDIAC TRANSPLANT NURSE COORDINATOR
OPERATING ROOM PROTOCOL cont.**

METHODS	KEY POINTS
5. Make the following preparations for surgery:	a) PVC feeding tube used as urinary catheter b) Routine Iodophor skin scrub
6. Cardiac transplantation is performed as soon as the donor heart is available. Donor and recipient surgeries may take place simultaneously	
7. Relay messages to family	By the circulating nurse. The chaplain will not be permitted in the room
8. Notify ICU of the progress in surgery	By the circulating nurse. The "Patient Record for Unit" will be sent in the usual manner
9. Transport patients to ICU	In a unit bed made with freshly laundered linen

IN-HOUSE CARDIAC PROCUREMENT OPERATING ROOM PROTOCOL

OBJECTIVE:

To provide a controlled environment in which organ recovery can be accomplished safely and smoothly

IMPORTANT POINTS:

1. Documents that must accompany the donor to the Operating Room:
 - Pronouncement and time of death, signed by two physicians other than operating surgeons
 - Coroner's Consent
 - Family Consent
 - Completed Deceased Patient List (if body will go to the morgue)
2. Persons not actively involved in the transplant will be limited to a maximum of three (to be determined by the operating surgeon). The circulating nurse is authorized to maintain control of personnel and traffic in the operating room

METHODS	KEYPOINTS
1. Receive notification	On call O.R. nurse is notified by Transplant Coordinator that a possible in-house cardiac donor has been identified
2. Notify O.R. nurses assigned to do in-house cardiac procurement	Nurses do not need to come in until confirmed information is received
3. Obtain the following information when confirmed notification has been received <ol style="list-style-type: none">a. Name, age and identification number of donorb. Location of donorc. Time of surgeryd. Name of surgeons and assistantse. Organs to be recovered	

**IN-HOUSE CARDIAC PROCUREMENT
OPERATING ROOM PROTOCOL cont.**

METHODS	KEY POINTS
4. Ask Pharmacy to prepare two 1-liter bags of cardioplegic solution (Adult); 2-500 ml bags (Peds) or 2-250 ml bags for infants (0-12 months).	Send one recipient IBM card. Keep Solution in O.R. refrigerator at 4°C
5. Prepare O.R. for cardiac and/or multiple organ procurement	Use an adjacent room for direct transfer of heart to recipient
6. Set up instruments with supplies	Provide separate tables for each team procuring an organ
7. Receive donor into operating room	Patient will be in supine position
8. Assist surgeon in preparing the heart for transplantation or for transport to another hospital	Circulating nurse clears subroom or hallway for surgeon to transfer heart aseptically to recipient room
9. Follow "Care at Time of Death" Technique to prepare the donor body (Technique D#11)	

DISTANT CARDIAC PROCUREMENT OPERATING ROOM PROTOCOL

OBJECTIVE:

To aseptically recover and transport a heart donated from another hospital to LLUMC-O.R. for transplantation.

IMPORTANT POINT:

Professional and courteous interaction with personnel in the distant hospital could positively influence future organ procurement.

METHOD	KEY POINTS
1. Receive notification. a) Notification of heart transplantation will be given to the nurse in charge carrying beeper 4531	On call O.R. nurse is notified by Transplant Coordinator that a possible distant cardiac donor has been identified
2. Notify O.R. nurse assigned to do distant cardiac procurement	Nurse does not need to come in until confirmed information is received
3. Obtain the following information when confirmed notification has been received:	
a. Name, age and weight of donor. 1) Identification number of recipient	For charging purposes when picking up cardioplegia solution in pharmacy
b. Name and telephone number of donor hospital	Telephone number necessary for communication regarding O.R. preparation
c. Expected time of departure	Needed so procurement nurse can determine time to arrive in operating room for assembly of procurement items
d. Type of transportation	Ambulance or limosine departs from ER; helicopter from the 7th floor heliport
4. Ask Pharmacy to prepare two liters of cardioplegic solution for adult patients; 2-500 ml for peds and 2-250 ml-bags for infants (age 0-12 months):	Send one recipient IBM card
5. Notify donor hospital operating room nurse to supply the following:	
1. Sterile sternal saw	
2. One bucket of crushed ice to pack the heart in ice chest for transportation	

**DISTANT CARDIAC PROCUREMENT
OPERATING ROOM PROTOCOL cont.**

METHODS	KEY POINTS
6. Prepare transplant suitcase and ice chest	<p>Suitcase: Sterile sternal saw as needed (battery-operated one is preferred), procurement instrument set (adult vs. peds), container for heart, red and green top test tubes (5 each)</p> <p>Ice Chest: 2-liter bags of cardioplegic solution (adult); 2-500 ml bag (pediatric); 2-250 cc-bag cardioplegic solution (infant); 6 liters (3-2000 ml bottles) cold saline; fill ice chest with crushed ice.</p>
7. Proceed to departure area with suitcase and ice chest	Ground transport departs from Emergency Room. Helicopter departs from 7th floor heliport
8. Identify donor by name and identification number upon arrival in donor hospital	Transplant Coordinator assumes responsibility for obtaining proper consents, verifying time of death and other required documents.
9. Scrub and set up instruments and supplies. Assist surgeon with cardiac procurement and packaging	Use separate table / Mayo tray from donor hospital's routine setup to expedite collecting LLUMC instruments and equipment at end of procedure. Follow "Cardiac Procurement Duties and Responsibilities" for scrub nurse (Cardiac Surgery Orientation Manual)
a) 10cc of 50% Dextrose should be placed in first ziploc bag with normal saline to fill bag about 2/3 full	
b) Place heart in solution and close bag	
c) Place ziploc bag in plastic container and seal lid	
d) Place plastic container inside bowel bag and tie shut	
10. Collect all instruments and equipment for return trip surgery to LLUMC	Transplant Coordinator communicates progress of procurement to LLUMC O.R.
11. Deliver heart to LLUMC O.R.	By procurement team. Heart is in ice chest
12. Clean, repack, and restock transplant suitcase using content list, and turn in appropriate supply charges	By procurement nurse. Use recipient IBM card for charges. Return supplies to transplant coordinator's office

**CARDIAC PROCUREMENT SCRUB NURSE
DUTIES AND RESPONSIBILITIES**

METHOD	KEY POINTS
1. Set up instrument table	1. Distant Procurement: ask for separate table/mayo tray for own instruments and supplies. Open 3 sterile basins on the table, fill with iced/cold saline
2. Drape the donor	2. See “Method of Chest Draping” Distant Procurement: follow the donor hospital’s routine
3. Pass the bovie suction tubing, cardioplegic tubing, pump tubing (if CPB is used)	3. Ask for separate bovie and suction for the cardiac team
4. Place 2 laparotomy sponges (adult), 2 4x4 gauzes(peds) on chest area. Skin incision made with #10 blade	4. Surgeon likes to wipe gloves with wet laps before making skin incision. (See Doctor’s Preference Card)
5. Hand sternal saw to surgeon	5. Test saw before the surgeon uses
6. Hand sternal spreader to surgeon	
7. Hand pericardial sutures to surgeon	7. Universal pericardial sutures: 2-0 silk, T-5 D-tach
8. Hand O-silk ties on the passer	8. With right angle, the O-silks are passed through the vessels. This is to mobilize the aorta, main pulmonary artery and superior vena cava
9. Prepare cardioplegic line	9. Cardioplegic purse string: 5-0 prolene T-16 cardioplegic needle: adult: #14 gauge angiocath 5_” or peds: #18 or #16 gauge angiocath 2”
10. Remove heart from the cavity	10. Surgeon uses scissors to do the cardiectomy
11. Rinse heart in cold saline	11. Heart is rinsed in 3 separate basins with cold/iced saline. Add 10 cc. 50% Dextrose to preservation solution *In house recipient: heart is transferred with the basin filled with cold saline (last rinsing basin) by surgeon to recipient’s room *Distant Procurement: heart is aseptically packed in heart container, put inside the ice chest and covered with crushed ice

**CARDIAC PROCUREMENT SCRUB NURSE
DUTIES AND RESPONSIBILITIES cont.**

METHOD	KEY POINTS
12. Close the chest	12. Done by the assistant or other organ procurement team *Distant Procurement: procurement nurse needs to pack the instruments and supplies and be ready to leave with the team
Note: Specimens needed for Immunology Center Blood: (2 red top and 4 green top vacutainers) Tissue: thymus, spleen and lymph nodes.	

CARDIAC PROCUREMENT CIRCULATING NURSE DUTIES AND RESPONSIBILITIES

METHOD	KEY POINTS
1. Prepare O.R. for organ procurement	1. In-house Recipient: prepare procurement room adjacent to recipient room. Keep O.R. temperature warm. Use K-thermia blanket, heating light (peds only, or per request of Anesthesiologist)
2. Receive donor in operating room	2. Identify donor through the I.D. band. - check donor's chart and obtain the following information: <ol style="list-style-type: none"> a. pronouncement and time of death, signed by two physicians other than the operating surgeons b. coroner's consent c. family consent d. completed deceased patient list
3. Proceed with routine preparations for surgery <ol style="list-style-type: none"> a) Obtain 2 bovie machines and 2 suction setups 	3. Skin prep: Cardiac Procurement only: from chin to umbilical line Multi-organ Procurement: from chin to mid-thighs. Use separate suction and Bovie machine for heart
4. Connect Sarn's saw to the motor, help run the foot pedal	4. Needs to be done as soon as the skin incision has been completed
5. Connect IV tubing/cardioplegic line to the cardioplegic solution bag	5. Cardioplegic solution is kept cold in the refrigerator/freezer
6. Pour cold/iced saline into the sterile basins (3 basins)	6. Use three-1500 ml saline containers. Make sure the saline is cold enough (4°C)
7. Clear the subroom/hallway for the surgeon to transfer the heart (in-house recipient)	
8. Complete paper work	8. Donor's chart needs to be sent out with the body
9. Prepare body according to "Care at Time of Death Procedure" (Technique D #11)	9. Out of state donor: communicate with transplant coordinator for the disposition of the body

PHYSICIAN POST-OPERATIVE ORDER SHEET (PEDIATRIC CARDIAC SURGERY)

POST-CARDIAC TRANSPLANTATION PHYSICIAN ORDER SHEET

DONOR RECOVERY PROTOCOL WHEN DONOR INFANT IS TRANSFERRED TO LLUMC

1. LLUMC neonatal transport team travels to donor point of origin (if donor is to be returned to LLUMC).
2. Documents needed before transport of donor:
 - a. Two signatures certifying brain death (preferably one from a pediatric neurologist) at donor point of origin (state laws may vary)
 - b. Death certificate signed at donor point of origin (if available)
 - c. Coroner's consent at donor point of origin
 - d. Family consent for donation (consent for transport to Loma Linda University Medical Center, if necessary)
 - e. Instructions as to handling and return of body
 - f. Permit to return the body (if crossing state lines)
3. Documents which must be with donor in transit:
 - a. Evidence of brain death confirmation
 - b. Death certificate (if available)
 - c. Coroner's agreement
 - d. Cardiac diagnostic studies
 - e. Consent for cremation, if indicated
 - f. Copy of donor chart
 - g. If body is to be returned across states lines, permission to embalm and burial certificate are required
4. Donor is transported to LLUMC and admitted to NICU
5. Donor evaluation by:
 - a. Neonatologist
 - b. Pediatric neurologist
 - c. Pediatric cardiologist
 - d. Pediatric infectious diseases specialist
6. Transfer donor to the operating room
7. The unit manager will make arrangements to return the body
8. The body must be embalmed to cross state lines on commercial airlines

PEDIATRIC TRANSPLANTATION VISITATION GUIDE

After your child has returned from surgery he/she will be kept in a protective isolation environment to help decrease the possibility of getting an infection while recovering from the stress of surgery.

Before you enter the room:

1. Wash from your hands to your elbows with a scrubbing motion, using special soap for three (3) minutes.
2. If you leave the room, the above step must be repeated before re-entering the room. (Note: Care must be taken not to touch any part of your face, hair, the floor or any other area that is considered to be "dirty." If these areas are touched, you must rewash your hands.)

We encourage you to visit your child whenever possible. Having your love and care is an important part of his or her recovery. Due to the lengthy preparation required to enter the room, you may find that less frequent but longer visits are best. Arranging visiting times with your child's nurse will allow your visit to be more relaxed, because it can be planned around your child's care and procedures.

We are happy to talk with you at any time (24 hours a day) if you have a question or concern about your child. It will decrease phone calls (to you and the unit) if you designate one family member as the spokesperson to keep your family updated on your child's condition.

Because of the protective environment and medication your child is on, we ask that only parents enter the room. Other family members can enter the ante room to "take a peek." Arrange this with the nurse. While in the ante room all the doors and windows are to be closed.

We encourage you to bring your child's favorite toy and clothes from home. These items are important to your child and you. They represent love, caring, and a link to home.

Prior to your child's discharge from the hospital, one parent will actually "live-in" to familiarize yourself with your baby's 24-hour schedule.

We want to make your experience with us as easy as possible. Please let us know how we can be of further help.

Welcome and thank you,
Nursing Staff

FAMILY ROOMING-IN

Parents are encouraged to spend a full 24-hour cycle with their infant prior to discharge to familiarize themselves with the baby's routine.

NURSING RESPONSIBILITIES

1. Obtain and write a baseline assessment including vital signs at the beginning of each shift
2. During AM and PM shifts demonstrate taking of vital signs and have parents do a return demonstration
3. Continue to document activity, rhythm strips, feedings, and I. & O. every shift
4. Demonstrate to the parents how to weigh the diapers and keep an I. & O. record
5. Weigh the child every AM before rounds and record in the bedside chart
6. Continue to update the care plan every shift
7. Check with the family at least every two hours (except at night) for any questions or concerns. (This gives the nurse a chance to observe parent-child interaction.) When rooming-in is ordered by the physician, arrange with the unit secretary for a bed to be put into the room and meal trays to be served to the parents as needed
8. See that medications are given and documented. Work with the parent to demonstrate proper dosage and administration
9. Educate the parents regarding the purpose and side effects of each medication. Have them be able to identify and administer medications. Discuss what to do in the event of vomiting after a medication is given, i.e., if vomiting occurred immediately after the medication is given, repeat the same dosage. If vomiting occurred more than one hour after a medication is given, repeat one-half of the original dosage
10. Review with the parents the signs and symptoms of rejection, using their discharge teaching manual
11. Review the supplies needed for discharge

At the end of the period of rooming-in, the parents will be able to:

1. Perform daily routine cares.
 - a. bath
 - b. feedings
 - c. incision care
2. Demonstrate the correct technique for obtaining and documenting temperature, pulse, and respirations
3. Demonstrate technique for and rationale of accurate intake and output documentation
4. Demonstrate proper administration of medications
5. State the purpose for and side effects of each medication their child is taking
6. State the signs and symptoms of rejection

DAILY FLOWSHEET FOR FOLLOW-UP CARE

METHOTREXATE TREATMENT GUIDELINES

RATIONALE

Refractory or recurrent rejection not responsive to the usual rescue therapy protocols of *Solumedrol* and anti-thymocyte serum, poses a serious, life-threatening problem for heart transplant recipients. Repetitive courses of steroid treatment increase the risks of adrenal suppression, delay bone growth and increase the risks of infection for these infants and children. Similarly, repetitive courses of anti-thymocyte sera increase the likelihood of developing anti-horse or anti-rabbit antibodies which may reduce effectiveness of therapy and increase the chances of an anaphylactic reaction. In addition, the risks of infection and lymphoproliferative disorders increase with multiple courses of therapy. To prevent significant deterioration in graft function and combat this resistant form of rejection, other forms of therapy must be considered.

Preliminary studies of adult transplant recipients with refractory rejection unresponsive to the usual immunosuppressive regimens have demonstrated some success with the use of *Methotrexate* (MTX) therapy. The rationale for the use of this drug was based on its use with certain disorders (e.g., rheumatoid arthritis and polymyositis) as well as its success in preventing graft-versus-host-disease after bone marrow transplantation. The success of MTX therapy in these situations probably results from not only its cytostatic properties but also its demonstrated ability to suppress production of antibody, and to increase the number of T-suppressor cells which may inhibit the allograft-specific cytotoxic cells. While the exact mechanism of action has not yet been elucidated, MTX therapy clearly has a variety of effects on both cellular and humoral immunity.

MTX therapy in the adult patients reversed the signs of rejection on biopsy in most patients treated, despite the fact that these patients had not responded to all other available therapy. However, rejection did recur in many of the patients requiring re-treatment with MTX. It is clear from the adult study that low doses of MTX are all that is required for effective therapy but the exact dosage regimen, dosing interval and duration of therapy required for maximal response with minimal side effects is not known.

While there are a variety of serious, even life-threatening potential complications of MTX therapy, the only one of significance which has arisen in the few adult patients treated thus far, has been a profound leukopenia. This has been associated with prolonged and elevated MTX levels in the blood of the affected patients. One adult patient with this complication developed overwhelming pseudomonas sepsis with in association with profound leukopenia. He succumbed to the infection.

Therefore, the adult experience gives reason for some hope for patients with refractory rejection but also has given concern about potential side effects. To date, pediatric experience with this therapy is even more limited. The proposed treatment regimen for pediatric patients with refractory rejection is based on the adult experience as well as the limited experience of a few pediatric transplant centers, including the LLUMC patient population.

METHOTREXATE TREATMENT GUIDELINES

INCLUSION CRITERIA AND WORK-UP FOR INITIATION OF THERAPY:

1. Infants and children considered for MTX therapy include the following:
 - a. Infants with multiple rejection episodes (requiring repeated dosing with steroids - i.e. more than two courses within two months or those who have failed to respond to at least one or more courses of *ATS* or *ATGAM*)
 - b. Infants or children with a single severely symptomatic (hemodynamically compromising) rejection episode who do not have symptomatic improvement or continue to worsen despite at least three or four days of combination steroid and *ATS* or *ATGAM* treatment
 - c. Infants or children with symptomatic rejection who cannot be treated with *ATS* or *ATGAM* due to pre-existing antibodies which would inactivate the drug or produce anaphylaxis
2. Monitoring during therapy:
 - a. Cardiac transplant rejection screen daily until one begins to see clinical improvement, then as dictated by clinical course but a minimum of twice weekly initially
 - b. CBC with differential and platelets daily if WBC is less than 4,000 cm/ml, ANC less than 2,000 cm/ml, or platelets less than 60,000 cm (weekly testing if minimum requirement)
3. Special circumstances:
 - a. Bone marrow suppression
 - 1) Maximal depression occurs about a week after dosing with *MTX*
 - 2) Significant leukopenia may necessitate reduction in dosage or temporary discontinuation of *MTX*
 - 3) Ulcerative stomatitis, pharyngitis, enteritis or GI bleeding may occur with leukopenia
4. Other side effects:
 - a. General: chills, fever, fatigue, dizziness, avascular necrosis of femoral head
 - b. Skin: Pruritis, urticaria, alopecia, phototoxic reaction, pain
 - c. GI: ulceration anywhere along GI tract, bleeding, anorexia, diarrhea, hepatotoxicity (fatty necrosis, fibrosis, cirrhosis)
 - d. Renal: cystitis, hematuria, azotemia
 - e. CNS: headache, dizziness, sleepiness, blurred vision, depression
5. Overdosage:
 - a. *Leukovorin calcium* (citrovarum factor) is an antidote when administered within 24 hours of overdose
 - b. Dose of *leukovorin* should be equal to or greater than *MTX* dose
 - c. May be given IV for first dose with IM injections every 6 hours x 4 doses
6. Drug interactions:
 - a. Increased toxicity potential:

METHOTREXATE TREATMENT GUIDELINES cont.

- 1) ASA
 - 2) Sulfonamides
 - 3) Barbiturates
 - 4) Dilantin
 - 5) Weak organic acids
- b. Reduced toxicity potential
- 1) *Tetracycline*
 - 2) *Trimethoprim*
 - 3) *Cephalothin*
 - 4) *Hydrocortisone*
 - 5) *Griseofulvin*
- c. Corticosteroids used concomitantly increase risk of serious complications
- d. Diuretics and CSA may prolong drug half-life by reducing renal excretion and decreasing tubular secretion of the drug
7. **Absolutely** contraindicated in pregnancy--may pose serious teratogenic risks to fetus
8. Exclusion criteria or related contraindication to *MTX*:
- a. Significant renal function abnormalities
 - b. Significant impairment of liver function:
 - 1) hepatitis
 - 2) cirrhosis
 - c. Severe anemia, leukopenia or thrombocytopenia
 - d. Active ulcer with bleeding
 - e. Active infection (CMV, bacterial infections, etc.)
 - f. Pregnancy (**MAY INDUCE SERIOUS TERATOGENIC EFFECTS ON FETUS**)
9. Pretreatment evaluation:
- a. Regular cardiac transplant rejection screen (EKG, echocardiogram, CXR, CFC, CBC, etc.) demonstrating rejection
 - b. Endomyocardial biopsy (if possible)
 - c. Absence of serious infection
 - d. CBC with differential and platelets
 - e. Renal function studies: urinalysis, BUN, creatinine, consider GFR
 - f. Liver function studies
 - g. Liver biopsy may be indicated
10. Proposed treatment regimen:
10 mg/m² given once weekly (every 12 hours x 3 doses) or every Monday-Wednesday-Friday or as a single dose.
If a child has hemodynamic compromise (i.e., a requirement for mechanical ventilation and/or inotropic support) when *MTX* is started, a one time course of *MTX* using an increased dosage schedule is initiated. This dosing schedule is 6.7 mg/m²/dose every 12 hours for 3 doses followed by 3.3 mg/m²/dose every 12 hours for an additional 3 doses; totaling 30 mg/m². This is followed by weekly maintenance therapy.

METHOTREXATE TREATMENT GUIDELINES cont.

METHOTREXATE REFERENCES

1. Roenigk H, Auerback R, Maibach H, Weinstein G: Methotrexate guidelines--revised. *Journal of the American Academy of Dermatology* February 1982; 2(6).
2. Gilbert S, Klintmalm G, Menter A, Silverman A: Methotrexate-induced cirrhosis requiring liver transplantation in three patients with psoriasis. *Arch Intern Med* 1990; 150: 889-891.
3. Robinson JA, Costanzo-Nordin MR, Grusk BB, Silver MA, Sobotka PA, O'Connell JB, Pifarre R: The use of low-dose methotrexate for the treatment of allograft rejection is associated with significant drug toxicity. *Bibliothca cardiol* 1988; 43:35-38 (Karger, Basel).
4. Olsen SL, O'Connell JB, Bristow MR, Renlund DG: Methotrexate as an adjunct in the treatment of persistent mild cardiac allograft rejection. *Transplantation* November 1990; 50(5):773-775.
5. Costanzo-Nordin MR, Bruska BB, Silver MA, Sobotka PA, Winters GL, O'Connell JB, Pifarre R, Robinson JA: Reversal of recalcitrant cardiac allograft rejection with methotrexate. *Supplement III Circulation* November 1988; 78(5):47-57.

TOTAL LYMPHOID IRRADIATION GUIDELINES (TLI)

INCLUSION CRITERIA

1. Chronic graft rejection confirmed with endomyocardial biopsy
2. Previous rescue therapy with polyclonal antibodies (or evidence of antibody formation) on multiple occasions
3. Maximal maintenance immunosuppression

EXCLUSION CRITERIA

1. Presence of posttransplant lymphoproliferative disease
2. Previous radiation

PROTOCOL FOR TLI

1. Notify Radiation Therapy (x44257) to arrange consultation
2. Physician obtains informed consent
3. Bi-weekly sampling of CBC and platelet count during TLI
4. Weekly sampling of CFC (T cell subsets) during TLI
5. TLI to deliver a total of 800 rads, with increments of 80 rads/day twice a week for a total of 5 weeks
6. Hold TLI if there is clinical or laboratory evidence of infection

AZATHIOPRINE (IMURAN) FORMULA

PRODUCT:	Azathioprine (Imuran) suspension	
FORMULATION:	For 10 mg/ml concentration	
	Tablets	QS to Conc.
	Dissolve tablets, after crushing, in 5-10 ml water.	
	Cologel	1/3 final volume
	Simple syrup	QS to final volume
STABILITY:	Do not refrigerate!	60 days
REFERENCE:	American Journal of Hospital Pharmacists, April 1983, Volume 40, No. 4 pps. 616-618 Contributor T	

NASHVILLE ANTITHYMOCYTE SERUM (ATS) Prophylaxis Protocol

PHYSICIAN GUIDELINES

1. Recipient age 0 to 18 years.
2. NKA to rabbits/Negative skin test
3. NKA or contraindications to premedication (Tylenol or Benadryl).
4. Signed "Consent Form".
5. Signed "Physician's Order" form with patient weight.

INDICATIONS

This protocol has, to date, been utilized in adults and in children for the treatment of acute graft rejection following renal, cardiac, bone marrow, and pancreatic transplantation. It has been used as prophylactic (induction) therapy following the above types of transplantation, as well as for the treatment of aplastic anemia.

CONSENT

Each patient is notified of the advantages, and possible disadvantages of N/R-ATS treatment prior to dosage. A consent form specific to this topic must be signed at this time, and kept as a part of the permanent record.

SKIN TESTING

Skin testing is performed prior to the first dose of each course of N/R-ATS. The skin test solution is mixed by combining a 1 ml. sample of N/R-ATS with 9 ml. of sterile, non-pyrogenic saline solution (0.9% NaCl) to make a 1:10 dilution of the ATS. The patient is tested with a 0.05ml. intradermal injection of this solution. The skin test site should be read 15 minutes after its administration. A local reaction of 10 mm. or greater with a wheal or erythema or both, with or without pseudopod formation and itching or a marked local swelling would be considered a positive test. It should be noted, however, that the predictive value of skin testing has not been proven clinically. Allergic reactions and on rare occasion anaphylaxis, have occurred in patients whose skin test was negative while patients with a positive skin test who have occasionally received N/R-ATS have tolerated the material well. Nevertheless, in the presence of a locally positive skin test to N/R-ATS, serious consideration should be given to alternative forms of therapy. The risk to benefit ratio must be carefully weighed. If therapy with N/R-ATS is deemed appropriate following a locally positive skin test, additional informed consent should be obtained from the patient and clearance from the local IRB secured. Treatment should be administered in a setting where intensive life support facilities are immediately available and with a physician in attendance familiar with the treatment of potentially life threatening allergic reactions. A systemic reaction such as a respiratory embarrassment, hypotension, or anaphylaxis precludes any additional administration of N/R-ATS.

N.B: We recommend skin testing prior to the first dose of each course of N/R-ATS only. We do not require that the skin test be repeated if a new lot number of N/R-ATS must be utilized during the prescribed course. We have established that the rabbit serum albumins and globulins remain consistent from lot to lot of N/R-ATS. Thus there is not enough variation in the antigenicity of different lots of N/R-ATS to warrant retesting.

NASHVILLE ANTITHYMOCYTE SERUM (ATS) Prophylaxis Protocol

DOSAGE AND ADMINISTRATION

N/R-ATS is administered in daily intravenous infusions of 0.1 to 0.5 ml. per kg. of body weight. N/R-ATS is dissolved in either normal saline (0.9% NaCl) or 5% Dextrose solution (D5/W). Recommended volume for the adult patient is 500 ml. This may be adjusted by the clinician according to patient need.

N/R-ATS should be infused into a high blood flow vessel, such as a central line or a large peripheral vein or dialysis access. It should be passed through a 0.22 or 0.45 micron in-line filter either as it is prepared in the pharmacy or during administration.

Generally, N/R-ATS dosage is initiated at 0.2 ml/kg., and is adjusted according to physiologic response. This response may be monitored by evaluation of graft function, or more directly, by the monitoring of absolute lymphocyte count or CD3 lymphocyte count. The absolute lymphocyte count should be reduced to below $200/\text{mm}^3$, and the CD3 lymphocyte count to below $150/\text{mm}^3$ within two to three days of therapy. If desired response is not seen, the dosage of N/R-ATS may be adjusted upward in increments of 50%, and then re-evaluated in two days.

Because of the possibility of allergic reaction, it is recommended that the first dose of N/R-ATS be administered in a setting in which the patient may be observed closely. During the first infusion of a course, the patient's vital signs should be monitored at least hourly. During subsequent doses, vital signs should be monitored immediately after the initiation, and at the conclusion of the infusion. Infusion should be stopped immediately if signs of respiratory distress or anaphylaxis occur. There should be a kit including medications for the emergency treatment of anaphylaxis at the bedside during each infusion of N/R-ATS. A kit in use at one center includes:

- 1) *Metaproterenol* Inhaler
- 2) *Benadryl* - 50 mg vials - #3
- 3) *Solucortef* - 1 vial
- 4) *Epinephrine* 1:1000 - 3 vials
- 5) 3 syringes with needles

The above medications are administered in the order listed. Persons administering N/R-ATS should be well trained in the recognition and treatment of anaphylactic reactions.

The N/R-ATS course should continue until, in the physician's evaluation, the desired clinical effect has been achieved, generally seven to fourteen days, or until alternative therapy has been chosen. N/R-ATS is often given concomitantly with other immunosuppressants, in accordance with the protocol of the individual physician and program.

N.B: Once diluted, N/R-ATS should be given within twelve hours.

ATS PROPHYLAXIS ORDERS

ATS PROPHYLAXIS ORDERS

ATS RESCUE ORDERS

ATS RESCUE ORDERS

ATGAM ORDER SHEET

ATGAM ORDER SHEET

SOLUMEDROL ORDER SHEET

PROSTAGLANDIN E-1 GUIDELINES

Because of its vasodilatory effects especially on the pulmonary vasculature and its proven immunosuppressive properties, infants undergoing heart transplantation will be maintained on *prostaglandin E-1 (PGE-1)* posttransplantation at the following regimen: starting dose is 0.05 mcg/kg/min to be weaned by 0.01 mcg/kg/min every other day until stopped completely after ten days.

Neonates undergoing heart transplantation will be weaned from PGE-1 as follows:

- 0.05 mcg/kg/min x 2 days
- 0.04 mcg/kg/min x 2 days
- 0.03 mcg/kg/min x 2 days
- 0.02 mcg/kg/min x 2 days
- 0.01 mcg/kg/min x 2 days, then discontinued

This is only a suggested protocol. The dose and length of therapy are left to the discretion of the attending physician.

GLOMERULAR FILTRATION RATES - NORMAL RANGES

<u>AGE</u>	<u>AVERAGE GFR ML/MIN/1.73 M²</u>	<u>RANGE ML/MIN/1.73 M²</u>
2-8 days	39	17-60
4-28 days	47	26-68
37-95 days	58	30-86
1-6 months	77	39-114
6-12 months	103	49-157
12-19 months	127	62-191
2-12 years	127	89-165

Reproduced with permission from Heilbron DC, Holliday MA, al-Dahwi A, Kogan BA. Expressing glomerular filtration rate in children, *Pediatr Nephrol.* 1991;5:5-11.

GUIDELINES FOR SANDOGLOBULIN (IVIG) INFUSION

DESCRIPTION AND INDICATION

Sandoglobulin is a polyvalent antibody product containing all IgG antibodies that regularly occur in the donor population. Sandoglobulin is indicated for the substitution treatment of patients who cannot produce enough IgG antibodies such as patients who have received immunosuppression therapy following organ transplantation.

DOSAGE AND ADMINISTRATION

Usual dose is 400 mg/kg/dose. Solutions come in 3%, 6%, 9% or 12%. For an initial infusion or in patients who have not received immunoglobulin in more than eight weeks, the recommended concentration is 12%; the rate should be increased slowly over 15 to 30 minutes as indicated by the physician. Reactions occur only 30 minutes to one hour following the beginning of the infusion.

NURSING CONSIDERATIONS

1. Start the infusion promptly following reconstitution
2. Monitor vital signs hourly from start to finish of infusion as a precaution against possible shock
3. Signs and symptoms of adverse reaction are:
 - a. Rise in temperature
 - b. Respiratory distress
 - c. Flushing
 - d. Chills or sweating
 - e. Drop in blood pressure 25% or more of baseline
4. If the above symptoms occur:
 - a. Stop infusion if still running
 - b. Give O₂
 - c. Notify cardiac transplant coordinator and give location of the child
 - d. Standard dose of *Benadryl* 1-2 mg IV slowly
Epinephrine 1:10,000 0.1 mg/kg IV may be given sequentially
 - e. Start *Lactate Ringers* 10 cc/kg IV

SANDOGLOBULIN ORDERS

DRUGS THAT ALTER CYCLOSPORINE LEVELS

Cyclosporine is extensively metabolized. *Cyclosporine* concentrations may be influenced by drugs that affect microsomal enzymes, particularly cytochrome P-450 III-A. Substances that inhibit this enzyme could decrease metabolism and increase cyclosporine concentrations. Substances that are inducers of cytochrome P-450 activity could increase metabolism and decrease *cyclosporine* concentrations. Monitoring of circulating cyclosporine concentrations and appropriate *Neoral*® dosage adjustment are essential when the following drugs are used concomitantly.

Drugs That Increase Cyclosporine Concentrations

<u>Calcium Channel Blockers</u>	<u>Antifungals</u>	<u>Antibiotics</u>	<u>Glucocorticoids</u>	<u>Other Drugs</u>
diltiazem nicardipine verapamil	fluconazole itraconazole ketoconazole	clarithromycin erythromycin	methylprednisolone	allopurinol bromocriptine danazol metoclopramide

Drugs That Decrease Cyclosporine Concentrations

<u>Antibiotics</u>	<u>Anticonvulsants</u>	<u>Other Drugs</u>
nafcillin rifampin	carbamazepine phenobarbital phenytoin	octreotide ticlopidine

Rifabutin is known to increase the metabolism of other drugs metabolized by the cytochrome P-450 system. The interaction between *rifabutin* and *cyclosporine* has not been studied. Care should be exercised when these two drugs are administered concomitantly.

Other Drug Interactions

Reduced clearance of *prednisolone*, *digoxin*, and *lovastatin* has been observed when these drugs are administered with *cyclosporine*. In addition, a decrease in the apparent volume of distribution of *digoxin* has been reported after *cyclosporine* administration. Severe digitalis toxicity has been seen within days of starting cyclosporine in several patients taking *digoxin*. *Cyclosporine* should not be used with potassium-sparing diuretics because hyperkalemia can occur. During treatment with *cyclosporine*, vaccination may be less effective. The use of live vaccines should be avoided. Myositis has occurred with concomitant *lovastatin*, frequent gingival hyperplasia with *nifedipine*, and convulsions with high dose *methylprednisolone*.

**MINIMUM BLOOD VOLUME REQUIREMENTS
FOR TRANSPLANT LABORATORY TESTING**

<u>TEST</u>	<u>AMOUNT</u>	<u>TUBE</u>
ABO Type & Cross	1.5 ml + few gtts	Red Top Tube Green
Aldosterone (Plasma)	3.0 ml	Green Top Tube on Ice
Amylase	1.0 ml	Red Top Tube
Anemia Studies:		
a) CBC with Platelets	0.5 ml	Lavender Bullet
b) Erythropoietin Level	2.0 ml	Red Top Tube
c) Ferritin	0.6 ml	Red Top Tube
d) HgB Electrophoresis	1.0 ml	Lavender Tube
e) Retic Count	0.5 ml	Lavender Tube
f) Serum Immunoglobulins A, E, G, M	3.0 ml	Red Top Tube
g) TIBC	1.0 ml	Red Top Tube
Anti-equine antibody	1.0 ml	Red Top Tube
Anti-rabbit antibody	1.0 ml	Red Top Tube
Basic Lytes	0.7 ml	Red Bili Tube
Bilirubin (T & D)	Infant: 2 Cap Tubes Child: 1.2 ml	Red Top Tube
Blood Cultures	0.5 ml each bottle	Pink & Yellow Bottles
BUN	0.6 ml	Red Bili Tube
Calcium	0.3 ml	Red Top Tube
Calcium (Ionized)	0.9 ml	Green Top Tube on Ice
Carnitine	2.0 ml	Green Top Tube
CBC with Platelets	0.5 ml	Lavender Bullet
CFC (Needs a CBC)	0.5 ml	Green Top Tube
Cell Profile	0.4 ml	Lavender Bullet
CK Isoenzymes	1.5 ml	Red Top Tube
CMV Ab Titer	0.6 ml	Red Top Tube
CMV IgG & IgM	2.0 ml	Red Top Tube
CMV Buffy Coat (Mon-Fri)	1.0 ml	Green Top Tube (Small)
CMV Titer	1.5 ml	Red Top Tube
Creatinine	0.3 ml	Red Bili Tube
Digoxin	0.3 ml	Red Bili Tube
Dilantin	0.15 ml	Red Bili Tube
Donor Specific Atb	0.2 ml	Red Top Tube
DPT Titer	1.0 ml	Red Top Tube
EBV IgG	1.0 ml	Red Top Tube
EBV IgM	1.0 ml	Red Top Tube
Erythropoietin	2.0 ml	Red Top Tube
Expanded Lytes	2.4 ml	Red Top Tube
FEP	1.0 ml	Lavender Top Tube
Ferritin	0.6 ml	Red Top Tube
Flecainide	1.5 ml	Red Top Tube
Free Thyroxine Index	0.6 ml	Red Top Tube
Gentamycin	0.3 ml	Red Bili Tube
Hemophilus Influenza Titer	1.5 ml	Red Top Tube
Hepatitis BsAtg	1.0 ml	Red Top Tube
Herpes Titer	2.5 ml	Red Top Tube
Hgb Electrophoresis	1.0 ml	Lavender Top Tube

**MINIMUM BLOOD VOLUME REQUIREMENTS
FOR TRANSPLANT LABORATORY TESTING cont.**

HIV	1.0 ml	Red Top Tube
IgE	0.9 ml	Red Bili Tube
IgG	0.9 ml	Red Bili Tube
IgM	0.9 ml	Red Bili Tube
Lipoprotein electrophoresis	2.0 ml	Red Bili Tube
Liver Profile	2.0 ml	Red Top Tube
Magnesium	1.0 ml	Red Top Tube
Myoglobin	1.0 ml	Red Top Tube
Osmolality (Serum)	1.0 ml	Red Bili Tube
Percent Reactive Atb	1.0 ml	Red Top Tube
Phenobarbital Level	0.2 ml	Red Bili Tube
Plasma Renin	3.0 ml	Special Lavender Tube
Potassium	0.3 ml	Red Bili Tube
Polio Titer	1.0 ml	Red Top Tube
Pneumococcal Ab Titer	4.0 ml	Red Top Tube
Procainamide	0.7 ml	Red Bili Tube
Protoporphyrin	3.0 ml	Lavender Top Tube
PSCE	2.7 ml +	Red Top Tube
	0.4 ml	Lavender Bullet
PT, PTT	2.7 ml	Blue Top Tube (Small)
Random Chem Profile	1.5 ml	Red Top Tube (Small)
Retic Count	0.5 ml	Lavender Bullet
RPR	0.7 ml	Red Top Tube
Serum Fe	0.6 ml	Red Top Tube
Serum Immunoglobulins (IgA, IgG, IgM)	3.0 ml	Red Top Tube
Sodium	0.3 ml	Red Bili Tube
Spontaneous Blastogenesis (Needs a CBC)	0.5 ml	Green Top Tube
TB Cell Enumeration	3.0 ml	Yellow Top Tube
TIBC	1.0 ml	Red Top Tube
Theophylline	0.2 ml	Red Bili Tube
TORCH	2.4 ml	Red Top Tube
Triglycerides (Fasting)	2.0 ml	2 Red Bili Tubes
TSH, T3, Free Thyroxine Index	3.6 ml	Red Top Tube
Vancomycin	0.7 ml	Red Top Tube
Varicella Titer	2.5 ml	Red Top Tube

CARDIAC TRANSPLANTATION AS TREATMENT FOR CHILDREN WITH LETHAL HEART DISEASE ASSOCIATED WITH ASPLENIA

Asplenia syndrome is defined as congenital asplenia with cardiac anomalies consisting of abnormalities of the atrioventricular canal, venous return (systemic and pulmonary), and/or conotruncal alignment. The association between agenesis of the spleen (asplenia) and cyanotic congenital heart disease has been well documented. Previously, it had been felt that the lack of splenic function and risk of infection would limit survival. However, the cardiac anomalies are characteristically complex, multiple, and lethal. The number and complexity of the cardiac lesions present in each case frequently preclude conventional surgical correction. In the subset of patients who survive infancy and who are candidates for complex palliation (Fontan procedure), a 65% mortality rate is reported. Thus, the majority of children in recent times with asplenia syndrome die in infancy or childhood from either heart disease or attempts to repair the structural lesions, not from infectious causes.

Analysis of mortality data shows that the largest number of patients with asplenia syndrome die from their cardiac disease during the first year of life. Those who survive the first 12 months of life are at greater risk from infection due to absent splenic function. The management of children with functional asplenia (sickle cell disease, trauma, etc.) and improved immunizations have led to a marked improvement in the prevention and treatment of bacterial infections in children with asplenia. The immunologic interaction between transplantation and asplenia is unknown.

Attention has been given to the spleen's contribution to host defense, particularly for clearing intravascular microorganisms, especially in the nonimmune host. In addition, the spleen appears to contribute to normal antibody production following an intravascular challenge. Therefore, the spleen's function has generally been felt to be a part of one of the two major aspects of immunity; "humoral immunity". The immunosuppressive medications used with transplantation generally interfere with the other component; "cellular immunity". Often, there is significant interaction between these two components of immunity.

An association between an increased incidence of life-threatening, overwhelming bacterial sepsis and asplenia has been made. The increased susceptibility to infection primarily involves young children prior to the acquisition of immunity for encapsulated organisms where splenic antigen processing contributes to acquired immunity. The risk of septicemia in hyposplenic disorders has been estimated at 15-50% greater than that expected in normal children. Therefore, asplenic patients need to be treated aggressively for possible bacterial infection. Newer vaccines for encapsulated organisms such as Hemophilus influenza capsular and pneumococcal polyvalent should be administered and penicillin prophylaxis is generally recommended for children with asplenia. Significant febrile episodes should be managed aggressively and the patient and family should be carefully educated about the risks of infection. Most deaths from hyposplenia-related septicemia are believed to be preventable.

With solid organ transplantation, there is increased concern about infection due to the immunosuppression of cellular immunity required for graft tolerance. However, there is a possibility that lack of splenic function may improve the host tolerance to the transplanted graft and thus require less immunosuppression.

LOMA LINDA UNIVERSITY MEDICAL CENTER AND CHILDREN'S HOSPITAL HEART TRANSPLANT PROGRAM

Quality Assurance Plan

Introduction:

The idea of assuring high standards of quality care in the Loma Linda Heart Transplant Program is not new. From its very inception, attention to detail and concern for assuring the best possible outcome have been foremost in everyone's thoughts and actions.

Survival statistics are probably the best indicator of a transplant program's quality of care, and these are followed closely, with review by state agencies and insurance programs. These reviews have been quite favorable and have resulted in formal recognition for Loma Linda as a transplant "Center of Excellence" and agreements to provide reimbursement for transplant services.

We have also been concerned that we are providing not just survival, but quality survival as well. As an example, studies looking at growth and developmental outcome in the pediatric age range have been done and are on-going.

There have been a number of studies looking at graft function, rejection screening, surgical techniques, etc. which have been presented in scientific forums, undergoing the scrutiny of the peer review process. The scientific method is QA at its best, for in it a problem or concern is identified, a hypothesis is generated, a plan is developed to test the hypothesis and then data is collected. And the peer review process is the primary mechanism in academic medicine of enhancing the principles and practices of medicine, both at the local institution and in disseminating information to other physicians and medical facilities.

A more formal process of quality assurance, though, is also indicated. This document will outline the quality assurance activities to date and present a framework for further quality assurance activities.

QA History:

In the early stages of the transplant process here at Loma Linda, each patient was intensely monitored. Using extensive data and experience derived from animal experiments, and experience gained from each transplant, protocols were developed. These protocols were constantly reviewed and modified as circumstances dictated. As the program has matured, the protocols have become more stable. And comparing different treatments has become somewhat easier with a larger patient base.

One of the most important aspects of the quality assurance process is the multi-disciplinary team approach. Very early in the process, a multi-disciplinary team conference was started. It continues to meet regularly. At this meeting, a review of the most recent developments on all of the surviving transplant recipients is performed as well as a comprehensive review of all new referrals and all patients on the waiting list. It also serves as a forum for morbidity and mortality review.

With this background in mind, the following describes the formal, on-going mechanism for assuring optimal quality care to our patients.

Quality Assurance Plan cont.

Statement of Purpose:

The ultimate purpose of the Quality Assurance Program of the Loma Linda Heart Transplant Program is the maintenance of the highest standards of patient care. Is designed to foster and monitor patient outcome and improve patient care both in the short and long-term.

Goals and Objectives:

The goals of the Quality Assurance Program encompass:

1. Providing a framework for the systematic, ongoing, and objective monitoring and evaluation of the quality of patient care.
2. Providing a mechanism of documenting ongoing Quality Assurance activities.
3. Providing an opportunity for a multi-disciplinary approach to Quality Assurance.
4. Providing a mechanism for identifying and solving perceived problems or concerns.
5. Providing a mechanism to evaluate the quality, content and completeness of medical record entries.

Authority and Responsibility:

The quality Assurance Program of the Loma Linda Heart Transplant Program has the support and approval of the Hospital Administration. The Medical Directors are responsible for the coordination of the program. The Hospital Quality Assurance Department will provide appropriate resources to assist in the implementation of the Quality Assurance Program.

Assuring quality care is the responsibility of every person involved in the care of the transplant recipient. Every opportunity to enhance care will be pursued and all matters which require additional support for resolution will be brought to the Quality Assurance Coordinator for action.

Organization:

1. Age Specific Transplant Patient Care Committees:

The pediatric committee meets on a weekly basis to discuss the most recent clinical course of, and make recommendations for, all surviving transplant recipients, all referrals and all patients on the waiting list. Significant morbidities and all mortalities are presented as well as special items of interest. Formal QA reports and clinical indicator monitoring will be discussed PRN. This committee is chaired by the Medical Director of the Pediatric Heart Transplant Program and includes Cardiothoracic Surgeons, Pediatric Cardiologists, Transplant Pediatricians, Neonatologists, Immunology, Pediatric Infectious Disease, Pediatric Endocrinology, Pediatric Nephrology, Transplant Coordinators, Social Worker and clinic personnel.

The adult committee meets monthly and as needed to discuss the most recent clinical course of, and make recommendations for, all surviving transplant recipients, all referrals and all patients on the waiting list. Significant morbidities and all mortalities are presented as well as special items of interest. Formal QA

Quality Assurance Plan cont.

reports and clinical indicator monitoring will be discussed PRN. This committee is chaired by the Medical Director of the Adult Heart Transplant Program and includes Cardiothoracic Surgeons, Internists, Cardiologists, Infectious Disease Specialists, Transplant Coordinators, Social Worker, Nurse Educator, and Nurse Manager from the nursing unit.

Quality Assurance Process:

There are several essential elements of the Quality Assurance Program. These can be summarized as follows:

1. Reviews are performed both retrospectively and concurrently.
2. Reviews must be clinically significant.
3. Areas targeted will focus on high volume, high risk and clinical outcome.
4. Reviews will include one-time reviews and ongoing clinical indicator monitoring.
5. Results of clinical indicator monitoring will be presented at the appropriate committee(s), actions taken and follow-up documented.
6. Clinical indicator monitoring will be reviewed periodically to insure continued clinical relevance.

Documentation:

As noted above, results of clinical indicator monitoring will be presented at the appropriate committee(s). These results will be documented in the pertinent minutes with review on a regular basis. These minutes will be maintained at the Transplant office for review by appropriate authorities when needed.

Quality Assurance Mechanism:

Concurrent Reviews:

1. Actuarial statistics will be presented quarterly.
2. A weekly review of the most recent data on each surviving transplant recipient, on each new referral and on every patient on the waiting list will be presented at the Transplant Patient Care conference. This will be documented in summary form in the minutes.

Ongoing Clinical Indicator Monitors:

1. Clinical indicator monitoring will be presented on a periodic basis.
2. Indicators of Care include:
 - Survival Statistics*
 - Length of Hospital Stay*
 - Freedom From Serious Renal Insufficiency*
 - Freedom From Negative Neurological Outcome*
 - Rejection*
 - Serious Infections*
 - Number of Pts Intubated > 5 days*
 - Rejection Rate*

Quality Assurance Plan cont.

Ongoing Clinical Indicator Monitors:

Rate of Re-hospitalization
Number of Days in Hospital-for 1st Post-Tx Year
Length of Waiting Period
0
Incidence of Coronary Artery Disease
Incidence of PTLD

New Problem Identification:

1. Periodically, new problems will be identified which will require an initial review and then subsequent action. These may or may not then need to be placed into the program as an ongoing clinical indicator.

REPORTING SCHEDULE

Month	Indicators
January	<i>Survival Statistics</i> <i>Length of Hospital Stay</i> <i>Freedom From Serious Renal Insufficiency</i> <i>Freedom From Negative Neurological Outcome</i>
February	<i>Rejection</i> <i>Serious Infections</i> <i>Number of Pts Intubated > 5 days</i>
April	<i>Survival Statistics</i> <i>Length of Hospital Stay</i>
May	<i>Rejection Rate</i> <i>Serious Infections</i>
June	<i>Rate of Re-hospitalization</i> <i>Number of Days in Hospital for 1st Post-Tx Year</i> <i>Length of Waiting Period</i> <i>Died while Waiting</i>
July	<i>Survival Statistics</i> <i>Length of Hospital Stay</i> <i>Freedom From Serious Renal Insufficiency</i> <i>Freedom From Negative Neurological Outcome</i>
August	<i>Rejection Rate</i> <i>Serious Infections</i> <i>Number of Pts Intubated > 5 days</i>
September	<i>Incidence of Coronary Artery Disease</i> <i>Incidence of PTLD</i>
October	<i>Survival Statistics</i> <i>Length of Hospital Stay</i>
November	<i>Rejection Rate</i> <i>Serious Infections</i>
December	<i>Rate of Re-hospitalization</i> <i>Number of Days in Hospital for 1st Post-Tx Year</i> <i>Length of Waiting Period</i> <i>Died while Waiting</i>

**LOMA LINDA UNIVERSITY MEDICAL CENTER
CLINICAL PATHWAY**

Diagnosis: Cardiac Transplantation - (Pediatric)

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-1
Neurological	<ul style="list-style-type: none"> • Neuro assessment every 1-2 hours • Observe for seizure activity secondary to rapid fluid shifts/ CSA toxicity/ effects of deep hypothermia and circulatory arrest • Sedation with MS/Versed • Phenobarbital prophylaxis for seizures 	<ul style="list-style-type: none"> • Neuro assessment every 1-2 hours • Sedation with MS/Versed • Begin weaning of sedatives in preparation for extubation 	<ul style="list-style-type: none"> • Neuro assessment 	<ul style="list-style-type: none"> • Neuro
Desired Outcome	Normal neurological status without deficit	Normal neurological status without deficit	Normal neurological status with increased activity	Normal neurological status with increased activity

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Dow
Cardiovascular	<ul style="list-style-type: none"> • Observe for effects of deep hypothermia, circulatory arrest and effects of rewarming (edema, injury to cell membranes, capillary leakage) • Observe for bleeding (heaviest bleeding due to CP bypass) • Monitor chest tube drainage • Replace intravascular loss as necessary with FFP, platelets, or RBC's • Continuous hemodynamic monitoring (CVP/A-line) • Monitor for arrhythmias • Vasopressor Therapy: Isuprel-very low dose for chronotropic effect (0.01 - 0.05 mcg/kg/min) <ul style="list-style-type: none"> -Dopamine-usually low dose at 2-5 mcg./kg./min. -PGE 0.05 mcg./kg./min. as a pulmonary vasodilator and immunosuppressant -May give Inocor for more depressed cardiac function. -Older children with right heart failure or persistent pulmonary hypertension may receive Priscoline 0.5 mg./kg./hr. -FFP and blood or 5 % albumin in addition to IV losses to maintain CVP if needed. • Monitor electrolyte balance (especially K⁺) 	<ul style="list-style-type: none"> • Continuous cardiac monitoring • Continuous hemodynamic monitoring (CVP/A-line) • PGE weaning protocol • Daily weights • Diuretic therapy • Cautious weaning of vasopressor support • Heart rate decreases to 80-120 (off Isuprel) (as donor heart recovers from ischemic stress, it can maintain cardiac output with slower endogenous rate) • Monitor chest tube drainage and replace with blood products as necessary • Fluid restriction 	<ul style="list-style-type: none"> • Continuous cardiac monitoring • Continuous hemodynamic monitoring (CVP/A-line) • PGE weaning protocol • Daily weights • Continue weaning vasopressors • Continue diuretics • Monitor chest tube drainage and d/c chest tubes when appropriate 	<ul style="list-style-type: none"> • Conti monit • Disc hemo monit (CVP/ • PGE protoc • Daily • Conti • Liber

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Dow
Desired Outcome	Control of bleeding; stable hemodynamic status with use of vasopressors	Stable hemodynamic status with minimal chest tube drainage	Stable hemodynamic status	Stable status;
Respiratory	<ul style="list-style-type: none"> • Monitor arterial blood gases frequently (There is a mixed respiratory and metabolic alkalosis secondary to hyperventilation, bicarbonate and diuretics) • Ventilator support-pressure limited time cycled ventilators for newborns; pressure cycled ventilators for older children • Use high pressure and low rates usually 24-30 PIP and 4-6 PEEP • Assess breath sounds every 2-4 hours • At risk for RV failure or persistent pulmonary hypertension • Daily CXR (may be more often at times) • Avoid aggressive suctioning which may promote PVR and cause pulmonary vasospasm • Continuous pulse oximetry • Observe for s/s of respiratory distress 	<ul style="list-style-type: none"> • Ventilator support continues • Daily CXR • Pulmonary toilette to avoid atelectasis • Chest P.T./suctioning/med neb. • Assess CXR for pulmonary edema secondary to thermal injury and fluid overload • Diuretic therapy for pulmonary edema and fluid overload • Wean FIO₂ while monitoring PaO₂ and pulse oximetry • Monitor blood gases and begin weaning from ventilator when awake. Depending on diuresis, may extubate on day 3-5 postoperatively • Assess breath sounds every 2-4 hours • Continuous pulse oximetry • Observe for s/s of respiratory distress 	<ul style="list-style-type: none"> • Monitor respiratory status: check, respiratory rate and effort, and ABG's • Daily CXR • Wean O₂ as tolerated: keep O₂ saturation > 95%, continuous pulse oximetry • Chest P.T./suctioning • Assess for upper lobe atelectasis after extubation • May require reintubation • May have increased difficulty if donor heart is larger which may cause pulmonary airway compression • Assess breath sounds every 2-4 hours • Observe for s/s of respiratory distress • Assess for pleural effusion 	<ul style="list-style-type: none"> • Monitor rate and effort • CXR weekly • Chest P.T./suctioning • Wear require maintain saturation continuous oximetry • Assess breath sounds every 2-4 hours • Observe respiratory

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Dov
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Desired Outcome	Stable ventilator status without acidosis; adequate oxygenation; maintenance of clear airway	Ability to wean from ventilator with adequate O ₂ saturation	Tolerates extubation without respiratory distress; adequate gas exchange	Supple weane
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System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Down
Gastrointestinal	<ul style="list-style-type: none"> • NPO • OG/NG tube to gravity drainage while intubated • Assess bowel sounds every 4-8 hours and prn • IV Ranitidine prophylaxis for ulcer prevention 	<ul style="list-style-type: none"> • NPO • OG/NG tube to gravity drainage while intubated • IV Ranitidine prophylaxis for ulcer prevention • Assess bowel sounds every 4-8 hours 	<ul style="list-style-type: none"> • D/C NG tube • Assess bowel sounds every 4-8 hours • Begin feeding a few hours after extubation (start with water then proceed or advance to formula or breast milk) • Assess for ability to take required oral fluids; implement gavage feeding as necessary • Observe for any pain which may interfere with nipple • Change to oral Ranitidine for ulcer prophylaxis. All other medications should be oral 	<ul style="list-style-type: none"> • Assess bowel sounds every 4-8 hours • Support oral intake as necessary • Encourage oral intake as tolerated • Oral ulcer prevention
Desired Outcome	No abdominal distention	No abdominal distention	Tolerating oral intake	Tolerating oral diet; no bleeding

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Dow
Renal/Metabolic	<ul style="list-style-type: none"> • Patient returns to ICU with serum glucose approximately 300 mg % which is similar to banked blood • Monitor blood glucose regularly as it falls to normal and IV glucose when it drops to approximately 100 • Monitor RBC, K⁻ and Ca⁺⁺ closely • Patients usually have had coarctation of the aorta and may be hypertensive (Rx Captopril/Enalapril/anti-renins) • Diuretics • May require peritoneal dialysis • K⁻ drip as necessary to maintain serum > 3.0 • IV fluids • Urinary catheter • Strict monitoring of I/O • Daily weight • Monitor BUN/Cr 	<ul style="list-style-type: none"> • Daily weight • Diuretics • Monitor RBS and K⁻ closely • IV fluids with fluid restriction (80 - 100 cc/kg/d) • Strict monitoring of I/O's • Observe for hypertension • Monitor BUN/Cr 	<ul style="list-style-type: none"> • Daily weight • Liberalize fluids once "dry" weight achieved • Monitor I/O • Observe for hypertension • Discontinue urinary catheter after diuretic phase 	<ul style="list-style-type: none"> • Daily • Asses GFR p central • Obse hypert
Desired Outcome	Metabolically stable	Metabolically stable	Metabolically stable	Metab

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Dow
Immune/Infection	<ul style="list-style-type: none"> •Protective isolation including: <ol style="list-style-type: none"> 1. Restrict traffic flow to ICU room 2. Restrict contact with ancillary persons 3. 3 minute scrub 4. Mask 5. Clean scrubs or cover gown •Observe for s/s rejection (Increased heart rate, increased respiratory rate, poor feeding, irritability, lethargy) •IV antibiotics (Kefzol) for prophylaxis with indwelling central lines •IV CSA - monitor levels daily •IV Azathioprine - monitor WBC •Acyclovir/Ganciclovir prophylaxis for CMV prevention •ATS induction x 5 days. Goal is to decrease incidence of rejection •Solumedrol 125 mg every 12 hours x 4 doses •IVIG for passive immune enhancement •Nystatin for thrush prevention 	<ul style="list-style-type: none"> •Protective isolation •Observe for s/s rejection •IV antibiotics for prophylaxis while central lines are in situ •IV CSA-monitor levels daily •IV Azathioprine - monitor WBC •Acyclovir/Ganciclovir prophylaxis continues •Nystatin prophylaxis •ATS protocol •IVIG as ordered 	<ul style="list-style-type: none"> •Protective isolation •Observe for s/s rejection •Prophylactic IV antibiotics continue •Change to oral CSA-monitor levels daily •Oral Azathioprine - monitor WBC •Acyclovir/Ganciclovir prophylaxis continues •ATS protocol •Culture all lines when d/c'd •IVIG as ordered 	<ul style="list-style-type: none"> •Prote •Obse rejecti •D/C •D/C •Oral •Moni •Oral monit •Acyc ir prop contin •Biop: clinica •Nysta
Desired Outcome	Patient will be free from infection; immune suppression will be balanced; no s/s of hyperacute rejection	Patient will be free from infection; immune suppression will be balanced	Patient will be free from infection; immune suppression will be balanced	Patient from i immun will be cathete negati

System	Immediate Recovery Phase	ICU-Vent Phase	ICU-Extubated Phase	Step-Dow
Education	<ul style="list-style-type: none"> • Psychosocial support to patient/family 	<ul style="list-style-type: none"> • Psychosocial support to patient/family 	<ul style="list-style-type: none"> • Psychosocial support to patient/family • Teach parents to give medicine • Teach parents to assess temperature, heart rate and respiratory rate • Parental involvement with feedings and activities of daily living 	<ul style="list-style-type: none"> • Psychol support patient • Parer medic: admin • Parer assess: temper and re: • Parer involv feedin of dail living • CPR parent:
Desired Outcome	Limit patient/family anxiety	Limit patient/family anxiety	Patient/family understands follow-up care and medications	Patient unders care ar

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Ackerman DL, Hopper AO, Emery JR, Deming DD. Heart transplantation causes prolonged but reversible suck/swallow dysfunction. *Pediatr Res* 1993 Apr;33(4):97A(166).
- Allard M, Assaad A, Bailey LL, et al. Surgical techniques in pediatric heart transplantation. *J Heart Lung Transplant* 1991 Sept/Oct;10(5):808-827.
- Alonso de Begona J, Gundry SR, Razzouk AJ, Boucek MM, Bailey LL. Prolonged ischemic times in pediatric heart transplantation: Early and late results. *Transplant Proc* 1993 Feb;25(1):1645-1648.
- Alonso de Begona J, Gundry SR, Razzouk AJ, Boucek MM, Kawauchi M, Bailey LL. Transplantation of hearts after arrest and resuscitation. *J Thorac Cardiovasc Surg* 1993 Dec;106(6):1196-1201.
- Alonso de Begona J, Gundry S, Kawauchi M, Bailey L, Gusewitch G, Fagoaga O, Chritton D, Folz J, Chang L, Darras D, Lebeck L, Nehlsen-Cannarella S. Assessment of baboon lymphocyte subsets and activity in cardiac xenobridging to allotransplantation. *Transplant Proc* 1992 Apr;24(2):453-454.
- Alonso de Begona J, Gundry S, Nehlsen-Cannarella S, Fullerton D, Kawauchi M, Razzouk A, Vigesaa R, Kanakriyeh M, Boucek M, Bailey L, Loma Linda University Pediatric Heart Transplant Team. HLA matching and its effect on infant and pediatric cardiac graft survival. *Transplant Proc* 1991 Feb;23(1):1139-1141.
- Alonso de Begona J, Kawauchi M, Fullerton D, Razzouk A, Gundry SR, Bailey LL. Heart transplantation in children. *Comprehensive Therapy* 1990;16(6):61-64.
- Ashwal S. Brain death in early infancy. *J Heart Lung Transplant* 1993 Nov/Dec;12(6):S176-178.
- Ashwal S, Caplan AL, Cheatham WA, Evans RW, Peabody JL. Social and ethical controversies in pediatric heart transplantation. *J Heart Lung Transplant* 1991 Sept/Oct;10(5):860-876.
- Ashwal S. Brain death in the newborn. *Clinics in Perinatology* 1989 June;16(2):501-517.
- Ashwal S, Peabody JL, Schneider S, Tomasi L, Emery JR, Peckham N. Anencephaly: Clinical determination of brain death and neuropathological studies. *Pediatric Neurology* 1990 July/Aug;6(4):233-239.
- Assaad A. Post-transplantation management of the newborn and the immunosuppressive role of Prostaglandin E. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S191-194.
- Assaad AN. Management of the newborn after cardiac transplantation. *J Heart Lung Transplant* 1991 Sept/Oct;10(5 Pt 2):823-24.
- Bailey LL, del Rio M. Transplantation for congenital heart disease. *Glenn's Thoracic and Cardiovascular Surgery*. 6th Ed. November 1995;Chap 94:1475-90.
- Bailey LL. Immunoregulative trends in pediatric heart transplantation. *Heart Surgery 1995*. Luigi C. D'Alessandro, ED. Rome, Italy:237-248.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Bailey LL, Gundry SR and Razzouk AJ. Heart transplantation among newborns. (Excerpta Medica-International Congress Series 1049, Bad Oeynhausen, Germany), Thoracic Organ Transplantation: *Routine As A Challenge* 1994:239-243.
- Bailey LL, Norwood W, Allan LD, Hammer CR, Annas GJ, Girvin JP, Capron A. Critical issues debates: Intervention for infants with fatal heart disease, xenografting, and brain death criteria for anencephalic infants. *J Heart Lung Transplant* 1993 Nov/Dec;12(6Pt 2):S351-378.
- Bailey LL. Heart transplantation techniques in complex congenital heart disease. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S168-175.
- Bailey LL, Gundry S, Razzouk A. Bless the babies, 115 late survivors of heart transplantation during the first year of life. *J Thorac Cardiovasc Surg* 1993 May;105:805-815.
- Bailey L, Gundry S, Razzouk A, Wang N, Loma Linda University Pediatric Heart Transplant Team. Pediatric heart transplantation: Issues relating to outcome and results. *J Heart Lung Transplant* 1992 July/Aug;11(4):S267-271.
- Bailey LL, Kahan B, Nehlsen-Cannarella S, et al. Neonatal immune system: Window of opportunity. *J Heart Lung Transplant* 1991 Sept/Oct;10(5 Pt 2):828-840.
- Bailey LL. Another look at cardiac xenotransplantation. *J Cardiac Surg* 1990 Dec;5(3):210-218.
- Bailey LL, Gundry SR. Hypoplastic left heart syndrome. *Pediatr Clin North Am* 1990;37(1):137-150.
- Bailey LL. Organ transplantation: A paradigm of medical progress. *Hastings Center Report* Jan/Feb Report 1990 Nov:24-28.
- Bailey LL, Wood M, Razzouk A, Van Arsdell G, Gundry S, Loma Linda University Pediatric Heart Transplant Team. Heart transplantation during the first twelve years of life. *Arch Surg* 1989 Oct;124:1221-1226.
- Bailey LL. Pediatric heart transplantation. *Ann Thorac Surg* 1989;48:612.
- Bailey LL. Donor organs from human anencephalics: A salutary resource for infant heart transplantation. *Transplant Proc* 1988;20(455):35-41.
- Bailey LL, Bui RB, Nehlsen-Cannarella SL, et al. Surveillance techniques in infant heart transplantation. Heart and heart-lung transplantation update, Italy. Proceedings of the First International Course on Heart, Heart-Lung, Liver and Pancreas Transplantation. *USES Edizioni Scientifiche Firenze* 1988;89-94.
- Bailey LL, Assaad AN, Trimm RF, Nehlsen-Cannarella SL, Kanakriyeh MS, Haas GS, Jacobson JG. Orthotopic transplantation during early infancy for incurable congenital heart disease. *Annals of Surgery* 1988;208(3):279-286.
- Bailey LL, Nehlsen-Cannarella SL, Jacobson JG. Allogeneic and xenogeneic heart transplantation in infants. *Recent Advances in Cardiovascular Surgery* Bruno Reichart, ED. Kastner & Callwey, Munich, 1988:27-31.
- Bailey LL. Biologic versus bionic heart substitutes. *ASAIO* Apr/June 1987;10(2):51-53.
- Bailey LL. Status of heart transplantation during early infancy. *Heart valve replacement: Current status and future trends*. (Eds) G Rabago and DA Cooley. Futura Publishing Company 1987:487-493.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Bailey LL. Clinical trials of cardiac xenotransplantation in newborns with hypoplastic left heart syndrome. *Pediatric Cardiology. Proceedings of the Second World Congress.* Springer-Verlag: New York, 1986: 682-684.
- Bailey LL, Nehlsen-Cannarella S. Observations on cardiac xenotransplantation. *Transplant Proc* 1986;18 (3 Suppl 2):88-92.
- Bailey L, Concepcion W, Shattuck H, et al. Method of heart transplantation used for treatment of hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg* 1986;92(1):1-5.
- Bailey LL, Nehlsen-Cannarella SL, Doroshov RW, et al. Cardiac allotransplantation in newborns as therapy for hypoplastic left heart syndrome. *N Eng J Med* 1986;315:949-951.
- Bailey LL. Role of cardiac replacement in the neonate. *Heart Transplant* 1985;4C5:506-509.
- Bailey LL, Nehlsen-Cannarella SL, Concepcion W, et al. Baboon-to-human cardiac xenotransplantation in a neonate. *JAMA* 1985;254:3321-3329.
- Bailey LL, Jang J, Johnson W, Jolley WB. Orthotopic cardiac xenografting in the newborn goat. *J Thorac Cardiovasc Surg* 1985;89(2):242-247.
- Bailey LL, Ze-Jian L, Jolley WB. Host maturation after orthotopic cardiac transplantation during neonatal life. *Heart Transplant* 1984;3:265-267.
- Bailey LL, Li Z-J, Lacour-Gayet F, et al. Orthotopic cardiac transplantation in the Cyclosporine-treated neonate. *Transplant Proc* 1983;15:2956-2959.
- Bailey LL, Huse WM, Wareham EE, et al. Experimental technique for perfusion for perfusion of the canine donor heart in vitro. *Arch Surg* 1970;100:129.
- Baum MF, Chinnock RE, Larsen RL, Whittaker-Allen JH, Ogata KK, Bailey LL. Intermediate follow up of somatic growth of infant heart transplant recipients. *J Heart Lung Transplant* 1996 Jan;15(1 Part 2):S82.
- Baum M, Chinnock R, Ashwal S, Peverini R, Trimm F, Bailey L. Growth and neurodevelopmental outcome of infants undergoing heart transplantation. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S211-217.
- Baum MF, Cutler DC, Fricker FJ, et al. Physiologic and psychological growth and development in pediatric heart transplant recipients. *J Heart Lung Transplant* 1991 Sept/Oct;10(5):848-855.
- Behrendt DM, Billingham ME, Boucek MM, Marxmiller JM, et al. Rejection/infection: The limits of heart transplant success. *J Heart Lung Transplant* 1991 Sept/Oct;10(5):841-847.
- Benson L, Freedom RM, Gersony W, Gundry SR, et al. Cardiac replacement in infants and children: Indications and limitations. *J Heart Lung Transplant* 1991 Sept/Oct;10(5):791-807.
- Berry GJ, Rizeq MN, Weiss LM, Billingham ME. Graft coronary disease in pediatric heart and combined heart-lung transplant recipients: A study of fifteen cases. *J Heart Lung Transplant* 1993 Nov/Dec;12(6):S309-319.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Bork J, Chinnock R, Ogata K, Baum M. Infectious complications in infant heart transplantation. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S199-202.
- Bork J, Baum M, Rincon D, Chinnock R and Lopez-McCormack C. Acute respiratory syncytial virus infection in infant heart transplant patients. *Clin Res* 1992 Feb;40(1):53A.
- Boucek MM, Mathis CM, Boucek RJ, Hodgkin DD, Kanakriyeh MS, McCormack J, Gundry SR, Bailey LL. Prospective evaluation of echocardiography for primary rejection surveillance after infant heart transplantation: Comparison with endomyocardial biopsy. *J Heart Lung Transplant* 1994;13(1):66-73.
- Boucek MM, Mathis CM, Kanakriyeh MS, McCormack J, Razzouk A, Gundry SR, Bailey L. Donor shortage: Use of the dysfunctional donor heart. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S186-190.
- Boucek M, Mathis C, McCormack J, Chinnock R, Gundry S and Bailey L. Cardiac transplantation in infants and children with anatomic and functional absence of the spleen (asplenia). *J Heart Lung Transplant* 1993 Jan/Feb;12(1 Pt 2):S92.
- Boucek MM, Mathis CM, Razzouk A, Gundry SR, Bailey LL, Fullerton DA, Campbell DN. Indications and contraindications for heart transplantation in infancy. *J Heart Lung Transplant* 1993 Dec/Nov;12(6 Pt 2):S154-158.
- Boucek M, Mathis C, McCormack J, Lopez-McCormack C, Baum M, Chinnock R and Bailey L. Effects of rejection on cardiac function: An age dependent spectrum. *J Heart Lung Transplant* 1993 Jan/Feb;12(1 Pt 2):S66(8).
- Boucek MM, Mathis CM, Lebeck LK, Nehlsen-Cannarella SL, Gundry SR, Bailey LL. Prophylactic antithymocyte serum reduces rejection frequency after pediatric heart transplantation. *J Heart Lung Transplant* 1992;11:205.
- Boucek MM, Mathis CM, Chinnock RE, Kanakriyeh MS, Nehlsen-Cannarella S, Gundry SR, Bailey LL, Boucek RJ. Polyclonal versus monoclonal anti-T cell antibody therapy in infant heart transplantation. *J Heart Lung Transplant* 1991 Jan/Feb;10(1):161A.
- Boucek MM, Mathis CM, Kanakriyeh MS, Gundry SR, Bailey LL. Late cardiac graft failure and hypertrophic ventricular outflow obstruction post infant heart transplantation. *J Heart Lung Transplant* Jan/Feb 1991; 10(1 Pt 2):163(37).
- Boucek MM, Kanakriyeh MS, Mathis CM, et al. Cardiac transplantation in infancy: Donors and recipients. *J Peds* 1990 Feb;116:171-176.
- Boucek MM, Hodgkin DD, Mathis CM, Kanakriyeh MS, Boucek RJ, Gundry SR, Bailey LL. Accuracy of echocardiographic rejection surveillance in infant cardiac transplantation. *J Heart Lung Transplant* 1990 Jan/Feb;(9)1:63(34).
- Bouchart F, Bailey L. Organ transplantation and tissue grafting. Research in organ transplantation tissue grafting: *Child Heart Transplantation and Results* 1994.
- Bouchart F, Gundry S, Van Schaack-Gonzales J, Razzouk A, Marsa R, Kawauchi M, Alonso de Begona J, Bailey L. Methotrexate as rescue/adjunctive immunotherapy in infant and adult cardiac transplantation. *J Heart Lung Transplant* 1994;5:427-433.
- Burton PBJ, Hauck A, Nehlsen-Cannarella SL, Gusewitch GA, Sorrensen CM, Gundry SR, Bailey LL. Hypoplastic left heart syndrome: Some clues to its aetiology. *Lancet* 1991;338(8775):1148.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Cervantes M. Psychological pediatric issues post-transplant: Survey says despite stress, parents would do it again. *Unos Update Journal* Sept/Oct 1993:10.
- Chandrasekaran K, Bansal R, Greenleaf J, et al. Early recognition of heart transplant rejection by backscatter analysis from serial 2D echos in a heterotopic transplant model. *J Heart Transplant* 1987;6:1-7.
- Chiavarelli M, Gundry SR, Razzouk AJ, Bailey LL. Operative procedures for infant cardiac transplantation. *Atlas of Heart and Lung Transplantation*, McGraw-Hill, Inc. New York: 75-85.
- Chiavarelli M, Gundry SR, Razzouk A, Bailey LL. Cardiac transplantation for infants with hypoplastic left-heart syndrome. *JAMA* 1993 Dec;270(24):2944-2947.
- Chiavarelli M, Bailey L, Loma Linda University Pediatric Heart Transplant Team. Neonatal heart transplantation indications and results. *Intrathoracic Transplantation 2000* ed. Kaye MP, O'Connell JB, Editors; Landes Co: Austin:110-116.
- Chiavarelli M, Boucek M, Nehlsen-Cannarella S, Gundry S, Razzouk A, Bailey L. Neonatal cardiac transplantation, intermediate-term results and incidence of rejection. *Arch Surg* 1992 Sept;127:1072-1076.
- Chiavarelli M, Gundry SR, Razzouk A, Bailey LL, Loma Linda University Pediatric Transplant Team. Some aspects of neonatal heart transplantation. *Heart Surgery* 1991;56:491-498.
- Chiavarelli M, Alonso de Begona J, Vigessaa RE, Gundry SR, Bailey LL, Loma Linda University Pediatric Heart Transplant Team. Heart transplantation in children. (Chapter, Mosby Year Book, St. Louis, MO) *Advances in Cardiac Surgery* 1991;3:155-174.
- Chinnock RE, Baum MF, Larsen RL, Shirali GS, Peverini RL, Johnston JK, Razzouk AJ, Gundry SR, and Bailey LL. Long term survivors of infant heart transplantation: Clinical outcome of 63 children who have survived greater than 5 years. *Pediatric Nephrology* 1996;3(4):C58.
- Chinnock RE, Larsen RL, Razzouk AJ, Ogata K, Baum MF, Gundry SR, Bailey LL. Cyclosporine monotherapy in young infant heart transplant recipients. *J Heart Lung Transplant* 1996 Jan;15(1 Pt 2):S81.
- Chinnock R, Torres V, Jutzy R, Johnston J, Larsen R, Razzouk A, Baum M, Janner D, Pediatric Heart Transplant Group-Loma Linda. Cardiac pacemakers in pediatric heart transplant recipients: Incidence, indications and associated factors. *PACE* 1996 Jan;19:26-30.
- Chinnock RE, Sherwin T, Robie S, Baum M, Janner D, Mellick L. Emergency department presentation and management of pediatric heart transplant recipients. *Pediatr Emergency Care* 1995 Dec;11(6):355-360.
- Chinnock RE, Emery J, Larsen R, Baum M, Janner D, Razzouk A, Gundry S, Nehlsen-Cannarella and Bailey L. Methotrexate therapy for complex graft rejection in pediatric heart transplant recipients. *J Heart Lung Transplant* 1995 Jul/Aug;14(4):726-733.
- Chinnock RE, Bailey LL. Medical examiners, coroners, and organ recovery in the United States. *JAMA* 1995 May;273(20):1578-1579.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Chinnock R, Bailey L, Sahney S, Nystrom G, Bork J, Baum M, Janner D, Larsen R. A randomized, prospective comparison of two post-transplant cyclosporine target ranges and their effect on rejection rate, renal side-effects and infections in the first 90 days after infant heart transplantation. *J Heart Lung Transplant* 1995 Jan/Feb;14(1 Pt 2):S62(107).
- Chinnock RE, Larsen RL, Emery JR, Bailey LL and the Pediatric Heart Transplant Team, Loma Linda. Pre-transplant risk factors and causes of death or graft loss after heart transplantation during early infancy. *Circulation* 1995;92(Suppl 2):I-206-II-209.
- Chinnock R, Peverini R, Johnston J, Zorn E, Thompson B and Bailey L. Hospital charges for infants undergoing cardiac transplantation for hypoplastic left heart syndrome. *Pediatr Res* 1994 Apr;35(4):32A.
- Chinnock RE, Baum MF, Larsen R, Bailey LL. Rejection management and long-term surveillance of the pediatric heart transplant recipient: The Loma Linda experience. *J Heart Lung Transplant* 1993 Nov/Dec; 12(6):S255-64.
- Chinnock R, Torres V, Jutzy R, and Johnston J. Cardiac pacemakers in infants and children undergoing orthotopic cardiac transplantation. *Eur JCPE* 1993 Sept; 3(3):A39(123).
- Chinnock RE, Johnston J, Baum M, Janner D, Robie S and Larsen R. Signs and symptoms of graft rejection in the infant heart transplant recipient. *Cardiology in the Young* 1993 June;3(Suppl 1):59.
- Chinnock R, Peverini R, Sahney S, Baum M, Robie S and Bailey L. Renal function after cardiac transplantation in infants. *J Heart Lung Transplant* 1993 Jan/Feb;12(1 Pt. 2):S76.
- Chinnock RE. Clinical notes: Follow-up care of the pediatric heart transplant recipient. Part I *Inland Pediatrics* 1992 April;6(8):3-4. Part II, *Inland Pediatrics* 1992 May/June;7(1):1.
- Chinnock R, Baum M, Lopez-McCormack C, Johnston J, Rincon D and Mace J. Follow-up care of pediatric heart transplant recipients at Loma Linda: A model emphasizing the role of the general pediatrician. *Pediatr Res* 1992 Apr;31(4 Pt 2):121A.
- Dajnowicz AM, Emery JR, Nystrom GA, Deming DD. Time to cardiac transplantation impairs neonatal head growth. *Clin Res* 1992;40(1):116A.
- del Rio M, Bailey L. Heart transplantation for congenital heart disease. *Glenn's Thoracic and Cardiovascular Surgery* Appleton & Lange, Editors 1996;91:1475-1490.
- del Rio M, Gundry SR, Razzouk AJ, Chinnock R, Bailey LL. Current status of neonatal heart transplantation. *Cardiac Surgery: Current Issues* 4, 1995:1-7.
- Drake B, Ashwal S, Schneider S. Determination of cerebral death in the pediatric intensive care unit. *Pediatrics* 1986;78:107-12.
- Eke CC, Gundry SR, Baum M, Chinnock R, Razzouk AJ, Bailey LL. Neurologic sequelae of deep hypothermic circulatory arrest in cardiac transplant infants. *Ann Thorac Surg* 1996;61:783-788.
- Emery, JR. Strategies for prolonged survival before heart transplantation in the neonatal intensive care unit. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S161-163.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Emery JR, Johnston JK, Murphy J, Parisi F, Peabody JL. Initiating the pediatric heart transplantation process. *J Heart Lung Transplant* 1991 Sept/Oct;10(5 Pt. 2):802-807.
- Emery JR, Johnston JK, Larsen RL, Peabody JL. Symptomatic restrictive foramen ovale not closure of the ductus arterioles is the leading cause of death in infants awaiting heart transplantation. *Pediatr Res* 1993 Apr;33(4):246A.
- Emery JR, Johnston JK, Peabody JL. Pre-operative outcome for newborns registered for heart transplantation. *Pediatr Res* 1993 Apr;33(4):246A.
- Fukushima N, Gundry SR, Razzouk AJ, and Bailey LL. Growth of oversized grafts in neonatal heart transplantation. *Ann Thorac Surg* 1995;60:1659-1664.
- Fukushima N, Kawauchi M, Bouchart F, Gundry SR, Zuppan CW, Ruiz CE, Bailey LL. Graft atherosclerosis in concordant cardiac transplantation. *Transplant Proc* 1994 June;26(3):1059-1060.
- Fukushima N, Gundry SR, Razzouk AJ, Bailey LL. Risk factors for graft failure associated with pulmonary hypertension after pediatric heart transplantation. *J Thorac Cardiovasc Surg* 1994 Apr;107:985-9.
- Fukushima N, Bouchart F, Gundry SR, Nehlsen-Cannarella S, Gusewitch G, Change L, Fagoaga O, Bailey LL. The role of anti-pig antibody in pig-to-baboon cardiac xenotransplant rejection. *Transplant* March 1994;57(6):923-928.
- Fukushima N, Gundry S, Razzouk A and Bailey L. Cytomegalovirus infection in pediatric heart transplantation. *Transplant Proc* 1993;25:1423-1425.
- Fullerton DA, Gundry SR, Alonso de Begona J, Kawauchi M, Razzouk AJ, Bailey LL. The effects of donor-recipient size disparity in infant and pediatric heart transplantation. *J Thorac Cardiovasc Surg* 1992;104:1314-1319.
- Grill BB, Bui HD, Klooster MK, Nehlsen-Cannarella SL, Mace JW, Toomey FB, Bailey LL. Virus-associated enteropathy: A frequent occurrence after cardiac allotransplantation in infants. *Clin Res* 1988;36(1):210A.
- Gundry SR, Fukushima N, Eke CC, Hill AC, Zuppan C, Bailey LL. Successful survival of primates receiving transplantation with "dead," nonbeating donor hearts. *J Thorac Cardiovasc Surg* 1995 June;109(6):1097-10.
- Gundry SR, Alonso de Begona J, Kawauchi M, Liu H, Razzouk AJ, Bailey LL. Transplantation and reanimation of hearts removed from donors 30 minutes after warm, asystolic 'death'. *Arch Surg* 1993 Sept;128:989-993.
- Gundry SR, Alonso de Begona J, Kawauchi M, Bailey LL. Successful transplantation of hearts harvested 30 minutes after death from exsanguination. *Ann Thorac Surg* 1992;53:772-775.
- Janner D, Bork J, Chinnock R, Baum M. Pneumocystis pneumonia in infant heart transplant recipients. (In Press, *Laryngoscope* 1996)
- Janner D, Bork J, Baum M, Chinnock R. Severe pneumonia after heart transplantation as a result of human parvovirus B19. *J Heart Lung Transplant* 1994 Mar/Apr;13:336-338.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Johnston JK, Chinnock RE, Zuppan CW, Razzouk AJ, Bailey LL. Limitations to survival for infants with hypoplastic left heart syndrome referred for transplantation: The Loma Linda Experience. *Pediatric Nephrology* 1996;3(4):C58.
- Johnston J. Xenotransplantation: Baboon to Human Heart. *Trends in Organ Transplantation*. B Williams, D Sanford-Guttenbeil, Editors. Springer Publishing Co. 1996;11:153-163.
- Johnston J. Successful cardiac transplantation in a premature infant with hypoplastic left heart syndrome: A clinical case presentation. *J Transplant Coordination* 1995;5:41-43.
- Johnston J. Transplant coordination. *Circle of Care* 1994 Summer:2-3.
- Johnston J. Cardiac transplantation in early infancy. *Critical Care Nursing Clinics of North America* 1992 Sept; 4(3):521-525.
- Johnston J. Role of the pediatric nurse in selection and support of potential donors for heart transplantation. *Focus on Critical Care* 1991 April;18(2):167-171.
- Johnston J. A new beginning: Current trends in pediatric heart transplantation. *Focus on Critical Care* 1991 Feb;18(1):23-28.
- Johnston J. Neonatal/infant heart transplantation. *Organ Transplant A Manual for Nurses*, Chapter 10. New York: Springer Publishing Company (1991):275-288.
- Johnston JK, Sakala EP, Loma Linda University Pediatric Heart Transplant Team. Neonatal cardiac allotransplantation facilitated by in-utero diagnosis of hypoplastic left-sided heart syndrome. *West J Med* 1990 Jan;152(1):70-72.
- Johnston J. Pediatric cardiac transplant coordinator. New specialty offers opportunity to shape the future. *Publications Career Research System, Inc.*, 1989-1990 Career Guide for Graduating Nurses.
- Johnston JK, Mathis CM. Determination of rejection using non-invasive parameters following cardiac transplantation in very early infancy--The Loma Linda Experience. *Prog Cardiovasc Nurs* 1988;3(1):13-18.
- Kanakriyeh MS, Boucek MM, McCormack J, Mathis CM, Moorehead SM, Bailey LL, Gundry SR. Late cardiac function in the distally procured graft post infant heart transplantation. *Am Coll Cardiol* 1991 Feb;17(2):170A.
- Kanakriyeh MS, Boucek MM, Thompson R, Petry EL, McCormack J, Zuppan GW, Hauck AJ, Mathis C, Gundry SR, Bailey LL. The incidence of coronary artery disease after pediatric heart transplantation. *JACC* 1990 Feb;16(6):174A.
- Kanakriyeh MS, Mathis CM, Boucek MM, McCormack J, Gundry SR, Bailey LL. Effect of donor size on graft function post infant heart transplantation. *J Heart Lung Transplant* 1990 Jan/Feb;9(1):77(92).
- Kanakriyeh MS, Mullins CE, Parisi F, Bailey LL. Late hemodynamic results after orthotopic heart transplantation for hypoplastic left heart syndrome. *Cathet Cardiovasc Diagn* 1989;18(4):232-236.
- Kawauchi M, Fukushima N, Gundry SR, de Begona JA, Nehlsen-Cannarella S, Bailey LL. Lymphocyte subset monitoring can detect xenoheart rejection in primates. *Transplant Proceed* 1994;26(3):1067-1069.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Kawauchi M, Gundry S, Alonso de Begona J, Razzouk A, Bouchart F, Fukushima N, Hauck A, Weeks D, Nehlsen-Cannarella S, Bailey L. Prolonged survival of orthotopically transplanted heart xenograft in infant baboons. *J Thorac Cardiovasc Surg* 1993 Nov;106(5):779-786.
- Kawauchi M, Gundry S, Alonso de Begona J, Fullerton D, Razzouk A, Boucek M, Nehlsen-Cannarella S, Bailey LL. Male donor into female recipient increases the risk of pediatric heart allograft rejection. *Ann Thorac Surg* 1993 Apr;55:716-718.
- Kawauchi M, Gundry S, Alonso de Begona J, Razzouk A, Bailey LL. Utilization of pediatric donors salvaged by cardiopulmonary resuscitation. *J Heart Lung Transplant* 1993 Mar/Apr;12(2):185-188.
- Kawauchi M, Gundry S, Beierle F, Alonso de Begona J, Bailey L. Myosin light chain efflux after heart transplantation in infant and children and its correlation with ischemic preservation time. *J Thorac Cardiovasc Surg* 1993 Mar;106(3):458-462.
- Kawauchi M, Gundry SR, Boucek M, Kanakriyeh MS, Alonso de Begona J, Vigesaa RE, Bailey LL. Real time monitoring of the endomyocardial biopsy site with pediatric transesophageal echocardiography. *J Heart Lung Transplant* 1992 Mar/Apr;11(2):306-310.
- Kawauchi M, Boucek M, Gundry SR, Kanakriyeh M, Alonso de Begona J, Razzouk AJ, Bailey LL. Changes in left ventricular mass with rejection following infant heart transplantation. *J Heart Lung Transplant* 1992 Jan/Feb;11(1):99-102.
- Kawauchi M, Gundry S, Boucek M, Bailey L. Transesophageal echocardiography in pediatric heart transplantation: Comparison to surface transthoracic echo. *Am Coll Cardiol* 1991 Feb;17(2):370A.
- Kawauchi M, Gundry SR, Alonso de Begona J, Beierle F, Bailey LL. Plasma level of FK 506 in newborn goats and infant baboons. *Transplant Proc* 1991 Dec;23(6):2755-2756.
- Kawauchi M, Gundry SR, Alonso de Begona J, Beierle F, Feikes R, Bailey LL. Xenotransplantation in newborn goats with FK506. *Transplant Proc* 1991 Dec;23(6):3293-3295.
- Kawauchi M, Van Arsdell G, Alonso de Begona J, Gundry SR, Bailey LL, Nehlsen-Cannarella S. Flow cytometric analysis of lymphocyte populations in FK506-treated newborn goats. *Transplant Proc* 1991 Dec;23(6):2970-2971.
- Kawauchi M, Gundry SR, Alonso de Begona J, Fullerton DA, Razzouk A, Boucek M, Kanakriyeh M and Bailey LL. Prolonged preservation of human pediatric hearts for transplantation: Correlation of ischemic time and subsequent function. *Surgery Forum* 1990;76:211-212.
- Larsen RL, Chinnock RE, VanderDussen L, Mulla NF, Shirali GS, Johnston JK, Razzouk A, Gundry S, Bailey LL. Previous cardiac surgeries: Effect on outcome of heart transplantation in children. *J Investigative Med* 1996;44:123A.
- Larsen RL, Applegate PM, Shah PM, Dyar DA, Ribeiro P, Chinnock RE, Mulla NF, Shirali GS, Kuhn M, Khan MA, Johnston JK, Fritzsche S, Robie S, Razzouk A, Gundry S, Bailey LL. Dobutamine stress echocardiography: Useful screening test for transplant coronary artery disease in children? *J Heart Lung Transplant* 1996 Jan:S70.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Lebeck LK, Chang L, Lopez-McCormack C, Chinnock R, Boucek M. Polyclonal antithymocyte serum: Immune prophylaxis and rejection therapy in pediatric heart transplantation patients. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S286-92.
- Martin RD, Parisi F, Robinson TW, Bailey LL. Anesthetic management of neonatal cardiac transplantation. *J Cardiothorac Anesth* 1989 Aug;3(4):465-469.
- Martin RD, Bailey LL, Jacobsen WK, et al. Anesthesia for neonatal orthotopic cardiac xenograft. *J Cardiothorac Anesth* 1987 April;1(2):132-135.
- Mathis CM, Kanakriyeh MS, Hauck A, McCormack J, Gundry SR, Bailey LL, Boucek MM. Accelerated graft atherosclerosis in infancy: A rare complication reflecting chronic rejection. *J Heart Lung Transplant* 1991 Jan/Feb;10(1):161(32).
- Matsumiya G, Nehlsen-Cannarella S, Gundry SR, Bailey LL. Baboon-to-human cardiac xenotransplantation in a neonate. Review of a case. *Trans Science*. (in press)
- Matsumiya G, Gundry SR, Nehlsen-Cannarella S, Fagoaga O, Morimoto T, Sadahiko A, Bailey LL. Over one-year survival of orthotopically transplanted monkey hearts in baboons: Analysis of contributing factors to acute rejections. *J Heart Lung Transplant* 1996;15(1 Pt 2):S93.
- Matsumiya G, Gundry SR, Nehlsen-Cannarella S, Fagoaga OR, Morimoto T, Arai S, Bailey LL. Serum interleukin-6 level after cardiac xenotransplantation in primates. *J Heart Lung Transplant* 1996:S61.
- Matsumiya G, Nehlsen-Cannarella S, Fagoaga O, Morimoto T, Arai S, Foltz J, Bailey LL. Successful long-term concordant xenografts in primates: Alteration of the immune response with methotrexate. *Trans Proc* 1996 Apr;28(2):751-753.
- Matsumiya G, Gundry SR, Fukushima N, Kawauchi M, Zuppan CW, Bailey LL. Pediatric cardiac xenograft growth in a rhesus monkey-to-baboon transplantation model. *Xenotransplant* 1996 June;3:76-80.
- Mulla N, Chinnock R. Pediatric Cardiac Emergencies: Managing children with congestive heart failure, hypercyanotic spells, and heart transplants in the ED. *Pediatric Emergency Medicine Reports* 1996;1(2):13-20.
- Mulla NF, Feenstra LH, Johnston JK, Larsen RL, Shirali GS, Ali Khan MA, Dyar DA, Chinnock RE, Bailey LL. Exercise capacity following neonatal cardiac transplantation for hypoplastic left heart syndrome (HLHS). *JACC* 1996;27:341A.
- Mulla NF, Lowewn NK, Beeson WL, Ogata K, Johnston JK, Khan MAA, Shirali GS, Larsen RL, Chinnock RE, Bailey LL. Endomyocardial biopsies in pediatric cardiac transplant recipients: Difficulties, complications and outcome. *J Investigative Med* 1996;44:122A.
- Mullen J, Bailey L, Razzouk A, Gundry S. Pediatric cardiac transplantation. *Seminar in Pediatric Surgery* 1993 Nov;2(4):254-264.
- Nehlsen-Cannarella SL, Chang L. Immunology and organ transplantation in the neonate and young infant. *Critical Care Nursing Clinics of North America* K Gould, A Johnson, P Hooper. WB Saunders, Editors Philadelphia 1992 June;4(2):179-191.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Nehlsen-Cannarella SL. Mother Nature's loophole: Unique features of the neonate's immune system and its maturation. *Amer Soc Clin Pathol Teleconference #8629* 1992;8629:1-38.
- Nehlsen-Cannarella SL. Mother Nature's loophole - Baby heart transplants. *Proceedings of American Institute for Oral Biology* 1989;46:46-49.
- Peabody JL, Emery JR, Ashwal S. Experience with anencephalic infants as prospective organ donors. *N Eng J Med* 1989 Aug;321(6):344-350.
- Razzouk AJ, Chinnock RE, Gundry RE, Gundry SR, Bailey LL. Cardiac transplantation for infants with hypoplastic left heart syndrome. *Progress in Pediatric Cardiology* 1996;5:37-47.
- Razzouk AJ, Gundry SR, Chinnock R, Larsen R, Johnston J, Ruiz C, Khan A, Bailey LL. Cardiovascular complications following heart transplantation in children: Recognition, management, and outcome. Presented at the 20th Annual Scientific Meeting of the American Society of Transplant Surgeons, May 18-20, 1994. (in press, *J Transplantation* 1995)
- Razzouk AJ, Chinnock RE, Johnston JK, Gundry SR, Bailey LL. Infant heart transplantation in the management of hypoplastic left heart syndrome. In: Anderson and Pozzi, Editors. *Hypoplastic Left Heart Syndrome*. Berlin: Springer Verlag London Limited, 1995. (in press)
- Razzouk AJ, Chinnock RE, Gundry SR, Johnston JK, Larsen RL, Baum MF, Mulla NF, Bailey LL. Transplantation as a primary treatment for hypoplastic left heart syndrome: Intermediate-term results. *Ann Thorac Surg* 1996;62:1-8.
- Razzouk AJ, Gundry SR, Chinnock RE, Larsen RL, Ruiz CE, Zuppan CW and Bailey LL. Orthotopic transplantation for total anomalous pulmonary venous connection associated with complex congenital heart disease. *J Heart Lung Transplant* 1995 Jul/Aug;14(4):713-717.
- Razzouk A. Surgical intervention in children after heart transplantation. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S195-198.
- Razzouk A, Bailey L. Infant heart transplantation. *Heart Disease in Infants, Children and Adolescents*. Moss and Adams, 1995;1(Part D)33:510-516.
- Razzouk AJ, Gundry SR, Bailey LL. Cardiac transplantation in infancy. *Cardiac Chronicle* 1990 Aug;4(8):1-6.
- Ruiz CE, Zhang HP, Larsen RL. The role of interventional cardiology in pediatric heart transplantation. *J Heart Lung Transplant* 1993 Nov/Dec;12(6 Pt 2):S164-167.
- Shirali GS, Dyar D, Beeson WL, Lombano F, Johnston J, Chinnock R, Mulla N, Kuhn M, Ali Khan MA, Bailey L, Larsen R. Left ventricular growth following infant heart transplantation - A five year follow-up study. Accepted, American Academy of Pediatrics 1996 Annual Meeting.
- Shirali G, Lombano F, Beeson L, Dyar D, Mulla N, Khan MAA, Chinnock R, Bailey L, Gundry S, Razzouk A, Johnston J, Larsen R. Does rejection affect ventricular remodeling following infant-pediatric heart transplantation? Presented, "Acute cardiac allograft rejection: New Insights." Milan, Italy, 17-19 Sep 95.
- Shirali GS, Lombano F, Chinnock RE, Larsen RL. Intermediate-term effect of allograft rejection on left ventricular remodeling following infant-pediatric cardiac transplantation. Submitted, JACC 1996.

Loma Linda University Medical Center and Children's Hospital
Heart Transplant Program
List of Publications

- Shirali GS, Cephus C, Dyar D, Lombano F, Mulla N, Kuhn M, Wood L, Chinnock R, Johnston J, Bailey L, Khan MA, Larsen R. Coarctation of aorta following infant/pediatric cardiac transplantation. *J Heart Lung Transplant* 1996 Jan;15(1 Part 2):S71.
- Shirali GS, Lombano F, Beeson WL, Dyar DA, Mulla NF, Khan MAA, Johnston J, Chinnock RE, Gundry SR, Razzouk AJ, Bailey LL, Larsen RL. Ventricular remodeling following infant-pediatric cardiac transplantation: Does age or size disparity matter? *Transplantation* 1995 Dec;60(12):1467-1472.
- Toomey FB, Bailey LL, Bui RB, et al. Chest radiography in infant cardiac allotransplantation. *Amer J Radiol* 1988;150:369-372.
- Trimm F, Ashwal S, Rincon D, et al. Infant cardiac transplant recipients: What is the neurodevelopmental outcome? *Clin Res* 1990;38(1):166A.
- VanArsdell G, Razzouk A, Chinnock R, Johnston J, Zuppan C, Gundry S, Bailey L. Pediatric heart transplantation. *Transplantation & Immunology Letter* 1993 June;9(2):9,17-19.
- Vricella L, Alonso de Begona J, Gundry SR, Vigessaa R, Kawauchi M, Bailey LL. Aggressive peritoneal dialysis for treatment of acute renal failure after neonatal heart transplantation. *J Heart Lung Transplant* 1992 Mar/Apr;11(2):320-329.
- Walpoth B, Nehlsen-Cannarella SL, Bailey LL. Xenotransplantation: Extended indications for pediatric cardiac transplantation. *Transplant Proc* 1986;18(453):43-44.
- Woo KT, Emery JR, Peabody JL. Cortical hyperostosis: A complication of prolonged prostaglandin infusion in infant cardiac transplant candidates. *Pediatrics* 1994 Mar;93(3):417-420.