

# Table of Contents

[Why Would A Child Need a Transplant? 5](#_Toc209002076)

[Diseases That May Be Treated with Lung or Heart-Lung Transplant 5](#_Toc209002077)

[World Experience in Lung Transplantation 6](#_Toc209002078)

[The Evaluation for Lung and Heart-Lung Transplantation 7](#_Toc209002079)

[Standard Pre-Transplant Testing: 7](#_Toc209002080)

[The Lung Allocation Score System 10](#_Toc209002082)

[Waiting Time On The List 11](#_Toc209002083)

[Where Do donor Lungs Come From? 11](#_Toc209002084)

[When Should I call the Transplant Team? 12](#_Toc209002085)

[Who Do I Call? 12](#_Toc209002086)

[What Happens When A Donor Becomes Available? 13](#_Toc209002088)

[What Information Can I Know About My Donor? 13](#_Toc209002089)

[What Can I do To Help My Child Prepare For Surgery? 14](#_Toc209002090)

[What About Support Group Meetings? 14](#_Toc209002091)

[What About Counseling? 14](#_Toc209002092)

[How Is The Surgery Done? 14](#_Toc209002093)

[How Long Will The Surgery Take? 15](#_Toc209002094)

[Surgical Incisions 16](#_Toc209002095)

[Blood Transfusions 16](#_Toc209002096)

[Pain Management 16](#_Toc209002097)

[What the PICU (Pediatric Intensive Care Unit) Will Be Like 17](#_Toc209002098)

[How Will Your Child Feel After The Surgery? 18](#_Toc209002099)

[What Happens On 3W? 21](#_Toc209002100)

[Complications 21](#_Toc209002101)

[Infections 21](#_Toc209002102)

[Rejection 22](#_Toc209002103)

[***Hyperacute rejection*** 22](#_Toc209002104)

[***Acute Cellular Rejection*** 23](#_Toc209002105)

[***Bronchiolitis Obliterans*** 24](#_Toc209002106)

[***Post-Transplant Lymphoproliferative Disease (PTLD)*** 26](#_Toc209002107)

[Immune Suppression 26](#_Toc209002108)

[***The Medications*** 27](#_Toc209002109)

[***Cyclosporine A*** 27](#_Toc209002110)

[***Azathioprine.*** 29](#_Toc209002111)

[***Mycophenolate Mofetil (CellCept).*** 29](#_Toc209002112)

[***Corticosteroids.*** 29](#_Toc209002113)

[***Sirolimus (Rapamycin).*** 30](#_Toc209002114)

[***Other medications frequently needed*** 30](#_Toc209002115)

[The First Three Months 30](#_Toc209002116)

[Instructions For Discharge 31](#_Toc209002117)

[Phone Numbers 35](#_Toc209002118)

[Frequently Asked Questions 35](#_Toc209002119)

*This book will provide the details about lung and heart-lung transplantation. Going through the process of transplantation is very difficult and confusing. It can be hard for families to understand what is going on. This booklet will give you something to write in, your questions, thoughts, and something to refer to. If things don’t make sense, make sure you clarify things with your doctor, the nurse coordinator, or the social worker.*

# Why Would A Child Need a Transplant?

Your child is being referred for a transplant surgery because his or her quality of life has been severely affected by a disease. Many types of lung disease may lead to end-stage lung failure. Your child has developed lung disease that neither medicine nor surgery are able to help. Patients are considered for lung transplantation when their lung disease cannot be significantly improved by either medical or surgical therapy. For some patients, the lung disease may also severely affect the function of the heart. This may mean that a heart-lung transplantation is necessary for your child.

Transplant is considered a treatment option when failure of the lungs and heart results in a poor quality of life and life expectancy is severely limited. Lung and heart-lung transplantation is a surgical and medical therapy that can lead to a better quality of life, improved lung function, and a chance for your child to experience normal childhood milestones.

# Diseases That May Be Treated with Lung or Heart-Lung Transplant

*Many different types of disease can lead to end-stage function of the lungs and the heart. In our center and across the U.S., the most commonly treated diseases include: Cystic Fibrosis, Primary Pulmonary Hypertension, Secondary Pulmonary Hypertension due to heart defects, Bronchiolitis Obliterans, and Interstitial Lung Disease.*

*There are three types of Lung Transplant: Heart-Lung, Double Lung, and Single Lung.*

***Indications for Single-Lung Transplantation:***

1. *Pulmonary Fibrosis*
2. *Pulmonary Hypertension*

***Indications for Double-Lung Transplantation***

1. *Pulmonary Fibrosis*
2. *Primary Pulmonary Hypertension and other types of pulmonary vascular disease*
3. *Interstitial Lung Disease*
4. *Cystic Fibrosis*
5. *Pulmonary hypertension with heart defects that can be surgically repaired*
6. *Surfactant Deficiency (due to ABCA3 mutations)*
7. *Surfactant Protein B and Surfactant Protein C Deficiency*
8. *Alveolar Proteinosis*
9. *Bronchiolitis Obliterans*

***Indications for a combined Heart-Lung Transplantation:***

1. *Pulmonary hypertension with structural heart defects that cannot be surgically repaired.*
2. *Patients with severe heart failure who also have one of the conditions listed above.*

# World Experience in Lung Transplantation

*The first successful heart-lung transplantation was performed in 1981. The first successful double –lung transplantation was performed at Stanford University by Dr. Bruce Reitz in 1985. The Registry of the International Society of Heart and Lung Transplantation maintains world-wide statistics for heart, heart-lung, and lung transplantation. Over 51,400 lung transplant procedures have been reported to the Registry since 1985. For children, 2,091 pediatric lung transplants and 689 pediatric heart-lung transplants were performed through 2014. The Lucile Salter Packard Children’s Hospital at Stanford University is the only pediatric lung transplant center in the Western portion of the United States. At LPCH, 114 have been performed since 1988.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | 1 Year | 2 Years | 5 Years | 10 Years |
| **Survival Rate After Transplantation** |  |  |  |  |
| **Double-Lung Transplant** | 75% | 62% | 45% | 30% |
| **Heart-Lung Transplant** | 70% | 50% | 40% | 25% |

# The Evaluation for Lung and Heart-Lung Transplantation

*Before your child is accepted for lung transplantation, a careful and comprehensive evaluation is necessary. The evaluation is done on site at The Lucile Salter Packard Children’s Hospital (LPCH) at Stanford University. The process takes approximately 3 days, is usually done outpatient, but this is based on your child’s medical condition. The evaluation process involves many studies. The purpose of these studies is to:*

* *Determine that no other medical or surgical therapy is possible and the lung
transplantation remains your child’s only best option for survival.*
* *Identify medical problems which would not benefit from lung transplantation, or pose too great of a risk for transplantation.*
* *Establish baseline medical, physical and psychological function for children who are candidates for lung transplantation. Many candidates will experience deterioration in function while waiting for lung transplantation.*
* *Educate you about lung transplantation.*

# Standard Pre-Transplant Testing:

* Electrocardiogram (EKG) - this test records the rhythm of the heart. It records how fast the heart is beating, and if there are any abnormal beats. It is done by placing sticker-type electrodes across your child’s chest.
* Echocardiogram (ECHO) - This test uses sound waves to look at heart size and how the heart muscle and valves are working. It is like an ultrasound.
* Cardiac catheterization—Patients with a history of pulmonary hypertension generally undergo these tests on an annual basis. It is used to measure the blood pressures in the lung and the heart. It is done with the patient under sedation administered by an anesthesiologist. A pediatric cardiologist inserts a catheter tube into the large vein or artery at the top of your child’s leg.
	+ Children 12 years and older who are being considered for lung transplant might not have to undergo this test if the ECHO seems to be very normal, and there are no other concerns for heart dysfunction. The measurement of these pressures is done in order to prioritize the sickest patients who will be treated with heart-lung transplantation.
* Transplant Education—your family will meet with one of our transplant doctors and transplant nurses to educate you about lung transplant, and answer any questions. We encourage you to ask the transplant team questions any time during the course of your stay.
* Clinical Social Work Assessment—your family will meet with our transplant social worker to review psychosocial issues and concerns, especially those which affect normal functioning and family issues.
* Dietary consultation—the dietician will perform an assessment of the weight, height, body muscle and fat stores, and will review your child’s dietary history in detail. Your child’s nutritional status is very important in maintaining health during the waiting period, lowering the risk of the surgery and aiding the recovery after transplantation.
* Neurodevelopment assessment—your family will meet with one of our pediatric psychologists to review cognitive (thinking skills) and emotional functioning of your child and your family as a whole. The stresses of lung transplantation make this an important and mandatory part of the evaluation.
* Financial Screening/Insurance Coverage—lung transplantation is covered by most insurance companies and medical assistance programs. An LPCH advisor will assist you in determining how the surgery and long-term medications will be paid. This is done before your child is evaluated.
* Child Life Services—one of the hospital’s child life specialists will meet you and your child and introduce you to their services. We use this to explain the process, tests, and procedures to your child in a way that might help them feel less nervous about an often traumatic hospital experience.



#

*After the initial transplant evaluation has been completed, the LPCH Lung Transplant Team will review the results of the studies to decide whether your child is a candidate who will benefit from lung transplantation. If so, your child will be listed with the United network for Organ Sharing (UNOS). UNOS lists organ transplant candidates by blood type, size, either lung prioritization score (for children under the age of 12 years) or by Lung Allocation Score (LAS) (children 12 years of age and older). Some families will relocate their homes closer to LPCH, but we will accept children on to the list who can arrive to the hospital within 4 hours. We usually recommend return visits every 3—6 months to assess how your child’s condition is changing.*

# The Lung Allocation Score System

*Each transplant candidate 12 years of age and older lung allocation score is calculated from the following diagnostic information:*

|  |  |  |
| --- | --- | --- |
| * ***Forced Vital Capacity***
 | * ***Pulmonary Artery Pressure***
 | * ***O2 saturation at rest***
 |
| * ***Age***
 | * ***Body Mass Index***
 | * ***Insulin-dependent diabetes***
 |
| * ***NYHA Functional Class***
 | * ***6-minute walk distance***
 | * ***Ventilator Use***
 |
| * ***Pulmonary Capillary Wedge Pressure***
 | * ***Creatinine***
 | * ***Diagnosis***
 |

*UNOS has devised a priority system for pediatric candidate lung offers. Allocation of lungs from donors under age 12, ages, 12— 17, and 18 and older, to transplant candidates will be prioritized as follows:*

|  |  |  |  |
| --- | --- | --- | --- |
|  | ***Donor Age < 12***  | ***Donor Age 12—17***  | ***Donor Age 18+***  |
| ***1st Priority Recipient***  | ***Age < 12***  | ***Age 12—17***  | ***Age 12+***  |
| ***2nd Priority Recipient***  | ***Age 12—17***  | ***Age < 12***  | ***Age < 12***  |
| ***3rd Priority Recipient***  | ***Age 18+***  | ***Age 18+***  |  |

# Waiting Time On The List

*Waiting times vary by age, blood type, height, and lung allocation score (or priority score). Due to minimal competition, the waiting time for infants and toddlers can range from days to a few months at the larger centers. Our center is in ‘competition’ with several heart and lung transplantation centers in California, Washington, and Colorado. Thus, small children can wait for up to two years for a transplant. Waiting times are generally shorter for patients waiting for double lung only compared to those waiting for a heart-lung transplantation.*

# Where Do Donor Lungs Come From?

*Organ donors are individuals in whom all brain function has stopped. This can occur after severe brain injury. Consent must be obtained for organ donation from family members or advance directives. Potential organ donors are evaluated carefully. Information collected includes their medical history, blood tests are obtained, and studies are done to look at the function of the organs to be donated (heart, lung, kidney, liver, pancreas). These tests are done at the hospital where the donor is.*

*The lungs in brain-dead donors are particularly susceptible to disease, and their function may worsen rapidly due to fluid build-up in the lung tissue, infection, or trauma. Only 20—40% of organ donors have lungs healthy enough to be harvested for transplantation. The number of donor lungs available is lower than the number of donor kidneys, livers, or hearts.*

*UNOS (United Network for organ Sharing) operates the Transplantation Network and keeps a registry of all patients waiting for any type of organ transplant in the United States. UNOS is a government-authorized organization which was established to provide fair distribution of organs to programs throughout the U.S.*

*CTDN (California Transplant Donor Network) coordinates all donor calls and possible transplant matches in the Bay Area and the surrounding counties. All areas of the country have an organ procurement organization like the CTDN to evaluate and coordinate organ donation.*

*When a lung or heart-lung block becomes available, the UNOS waiting list is checked (by blood type, size, date of listing or point score total) to see which patient is at the top of the list. The donor coordinator then contacts the transplant program to see if they would accept the organ(s) for that patient. If not, the next patient’s center is contacted. This process continues until the organs are accepted. The three chest organs (two lungs and a heart) may be used in three different patients from three different transplant centers, though single lung transplantation is rare in children. This complex process requires the utmost efficiency since the lives of several potential organ recipients are at stake.*

# When Should I call the Transplant Team?

* *Whenever there is any significant change in your child’s health status.*
* *Whenever your child develops an infection, is started on antibiotics, or there is a major change in medication, which includes being started on prednisone. Your doctor should always be alerted to new symptoms and should contact the transplant team.*
* *Whenever your child is admitted to the hospital for any reason.*

# Who Do I Call?

*Your primary contact will be Jennifer Shek, our lung transplant nurse coordinator. Her phone number is 650-380-1999.*

# What Happens When A Donor Becomes Available?

*When a suitable donor becomes available, we will call you. If you cannot get good reception with your cell phone, please call the LPCH operator at 650-497-8000 once you get to a better spot, or provide the number of a reliable land line. Tell the operator that your child is waiting for a lung transplant and that you were called and need to talk with the pediatric cardiothoracic transplant surgeon or Dr. Conrad. The operator will connect you.*

*When we call you, your child should not eat or drink ANYTHING. If your child takes coumadin we will instruct you NOT to give your child any. Before your child is listed as an active transplant candidate, arrangements must be in place to arrive at the hospital within 4 hours.*

*You will first go to the admitting department on the first floor. Your child will be admitted to a Nursing Unit on the general pediatrics ward prior to the transplant. Blood work drawn, a chest x-ray done, and a history and physical examination will be done.*

*• “DRY RUNS”—sometimes the donor lung doesn’t look healthy anymore, and the surgery will be called off. We only accept suitable organs, and information can become available even at the last minute (and a patient might already be in the operating room).*

# What Information Can I Know About My Donor?

*Curiosity about the donor is natural. Some people may think or dream about their donor. Some patients and families may wish to know about their donor, and some do not. It is natural to feel grateful to the donor family. However, because of the rules of patient confidentiality, we cannot provide information on the identity or circumstances of the death of the donor. Under certain circumstances, a donor might be considered a ‘high-risk’ donor, and your consent must be obtained before accepting that donor.*

*If you wish, you can write an anonymous letter to the donor family and give it to your transplant nurse or the social worker to pass through CTDN and on to the donor family. Donor families are often extremely appreciative of letters coming from organ recipients. If you write a letter, you can include first names only, no phone numbers, no addresses, and you must not make reference to your location. You may send pictures if you would like.*

# How to Help Prepare Your Child For The Surgery

*Patients who are on the waiting list for lung transplantation should participate in a pulmonary rehabilitation program. This regular exercise program is a great way to get in the best possible shape before having transplant surgery. The more fit a patient is going into surgery, the easier the recovery is likely to be. For patients with pulmonary hypertension, the exercise program will be specially ordered according to your child’s condition in conjunction with the recommendations of the pediatric cardiologists and pulmonologists.*

# What About Support Group Meetings?

*Any patient who is being evaluated for lung or heart-lung transplantation, who is on the transplant list awaiting a transplant, and patients who have received their lung transplant, plus their family members, are welcome to speak with our Social Worker, Tamzen Hull, about attending a general group (all types of recipients, pre- and post-transplant) or arranging a meeting with another family.*

# What About Counseling?

*Individual or family counseling is often recommended before transplantation, and is a required element of post-transplant care. There are so many stressors and adjustments with transplantation that it is helpful to discuss these with a therapist or counselor. Counseling can help families to communicate better and prepare for or cope with the many changes and uncertainties that can happen with this very stressful and complicated time.*

# How Is The Surgery Done?

*After the chest is opened the patient is placed on a heart-lung bypass machine. The heart-lung machine is able to do the work of both the heart and the lungs for the patient during surgery. This is how your child’s own heart and/or lungs are removed without harm. For heart-lung transplants, the donor heart and lungs come together as a single unit. It is sewn in place by the surgeon by connecting the end of your child’s own trachea to the donor trachea. The donor aorta (main blood vessel leaving the heart to the body) is attached to your child’s aorta, and the upper chamber of the right side of the heart (the right atrium) of the donor is attached to the recipient’s.*

*For lung transplants, the two lungs are separate. The airways of the donor are cut at the beginning of the right and left main bronchi. The blood vessels (pulmonary arteries and pulmonary veins) of the donor are attached to your child’s own pulmonary arteries and veins.*



Front view of the lungs and the heart. Back view of the lungs and the heart.

*After the lungs are in place, the surgeon will place 3-4 drainage tubes (2 on each side) to remove blood that collects in the chest cavity after surgery, and also to help the new lungs stay inflated. The chest tubes will be needed for about 2—7 days.*

*If your child doesn’t already have one, a semi-permanent central IV catheter, called a subclavian IV catheter, will be placed in the operating room just prior to surgery. This is necessary access to have in order to give post-operative medications and is also handy for blood draws. It will remain for about 1-2 weeks after the transplant. Your child will require daily or frequent IV medications and undergo many blood tests for the first month after transplantation. To minimize pain and anxiety associated with blood tests, then a semi-permanent catheter called a PICC line will be placed.*

# How Long Will The Surgery Take?

* *It takes about 1 hour for the anesthesiologist to put your child to sleep and to then insert the multiple necessary monitoring and IV catheters.*
* *A double lung or heart-lung transplant operation takes about 4—6 hours. If your child has had previous chest surgery done or cystic fibrosis, the surgery can take an additional 1—5 hours.*

#

# Surgical Incisions



The median sternotomy incision for the double lung and heart-lung procedures.

The ‘clam-shell’ incision for the double lung procedure, this incision is done in certain cases.

# Blood Transfusions

*Your child will likely receive blood products in the operating room and in the immediate postoperative period. The danger of transmitting infection to your child from blood transfusions is very low, because of the current blood screening technology and added precautions used in the transplant setting. It is not practical for you or your family members to donate blood for the transplantation because we do not know when the transplantation is going to take place. But, after the surgery, your child may need another transfusion, and there may be an opportunity to have friends or family members donate their blood for your child.*

# Pain Management

*It is essential for your child to become mobile as soon as the first day after the surgery. This helps keep the lungs well-inflated and prevent mucus plugging and pneumonia. But, it can be quite difficult to move or take deep breaths after a major surgery in the chest.*

*Your child might have an epidural catheter placed while in the operating room or soon after admission to the PICU to help control pain from the surgical incision and from the chest tubes that are present, 2 on both sides. This helps to minimize how much IV pain medication is needed, and minimizes the sedation that can occur with pain medications.*

# What the PICU (Pediatric Intensive Care Unit) Will Be Like

*Your child will likely have many IV lines, tubes, and other articles attached to him or her.*

*This picture is typical for a post-operative patient.*

*A breathing tube will be placed in your child’s mouth that goes into the trachea. Your child will not be able to talk or eat with this tube in place. The nurses and doctors in the PICU will communicate with your child by asking yes and no questions. Your child will likely be able either to nod his head, or write on a paper. The nurse and respiratory therapist (RT) will clear mucus out of the tube frequently, since your child will find it difficult to cough with the tube in place.*

*After the tube is removed, it is ESSENTIAL that your child coughs and breathes deeply to help mobilize the secretions inside the lungs. We will encourage your child to sit up and transfer to a chair as soon as he is able to. This simple activity helps to clear mucus from the lungs, and keeps the muscles of the body from getting too weak. Weakness worsens quickly if a patient doesn’t mobilize soon after surgery.*

* *Oxygen will be given as needed.*
* *Wrist restraints are often placed as a precaution so that children do not pull or dislodge the breathing tube or other IV catheters while they are waking up.*
* *Chest tubes (4-5 drainage tubes coming from your child’s chest). These are for drainage of blood and fluids from the surgery, and to help keep the lungs fully inflated. Usually, they are removed within 2—7 days.*
* *Foley catheter — a urine catheter to drain your child’s bladder. It is critical to monitor your child’s urine output in the first 24—48 hours after surgery. The tube is usually removed 2—4 days after surgery.*
* *Large IV catheters — these will be placed in your child’s arms, hands, or feet in addition to the subclavian catheter. Access to many veins is essential.*
* *PICC line — this will remain for the first several weeks after the surgery, since your child may need to receive long-term IV medications after the surgery, and also to provide a site for blood draws, since your doctor will be monitoring many different blood tests and medications after the surgery to check for proper medication dosing, infection, and toxicity of the immunosuppressants.*
* *Post-transplant patients are placed in isolation to protect them against infections. Your child will be in a single patient room during the transplant hospitalization. Hand washing by ALL visitors and family must be done on each visit and entry into the patient’s room.*
* *Recovery in the PICU is stressful and tiring to your child. We request that visitors be limited to the most immediate family members.*

# How Will Your Child Feel After The Surgery?

*After surgery, it is common to feel any or all of the following:*

1. *Lack of sleep—in the PICU, it is impossible to get uninterrupted sleep, because your child is being very closely monitored. Often, days and nights get confused. Sedation might be needed to re-establish a normal sleep-wake cycle.*
2. *Strange Dreams/Nightmares—Anesthesia, medications, lack of sleep, and other reasons can cause patients to have these problems, even hallucinations. We will need your help in interpreting your child’s moods and needs.*
3. *Pain/Discomfort—In the first 24 ours, pain is not usually a problem because the anesthesia received during the surgery acts as pain medication. After the first day, when your child begins to move and sit in a chair, they will feel pain at the site of the incision, and also will feel the discomfort of the breathing tube and the chest tubes that are in between the ribs. Pain medications will be ordered, and some patients may benefit from an epidural catheter placement.*
4. *Nausea/Poor appetite—medications, anesthesia, and surgery will often cause your child to feel nauseated. Medication to help the stomach empty and to increase activity of the intestine is often needed. Nausea and poor appetite will persist if your child is inactive or requiring frequent dosing with pain medications. The immunosuppressant medications can also cause this problem.*
5. *Difficulty concentrating—this will improve with time.*
6. *Weakness/Dizziness—the first few times out of bed will be difficult, and nurses and the physical therapists will assist your child until he is stronger and feels comfortable enough to walk on his own.*

*Once your child has been taken off of the ventilator, and seems somewhat better, he or she will be transferred to 3W, the nursing unit that all transplanted patients stay. Usually, the stay is between 1—2 weeks after the ICU transfer.*

***The thing about coughing***

Coughing is the lungs’ and body’s most important defense mechanism to protect against infection. Coughing also helps to keep the lung segments inflated with air and clear of mucus. One of the side effects of lung transplantation is that the nerves that used to go to your child’s native lungs have been cut. This is unavoidable in transplant. Patients often feel some chest wall pain and muscle weakness for some time. This will lead to shallow breathing and ineffective cough. If your child can’t cough deeply, secretions will get trapped, and your child might develop either an infection, or the need for oxygen, or require mechanical ventilation, or all of the above. As soon as your child has the breathing tube removed in the PICU, we will have your child use an incentive spirometer and a cough assisting device to help him breathe deeply and cough out mucus. He will need to do this 10 times an hour while he is awake. This is an extremely simple and effective way to avoid the problems stated above.

#

# What Happens On 3W?

*It is an adjustment period going to the ‘regular’ medicine ward from the PICU. In the PICU, you had a nurse in your room for most of the time. On the ward, your nurse will have 2 or 3 other patients to look after in addition to your child.*

*Visitors and staff are required to wash their hands and may have to wear a gown and gloves as soon as they enter your child’s room. Your child will be required to wear a special mask to wear when he leaves the room. This is to protect him from acquiring an infection. Remember, at this point they are immune-suppressed. Your child will tire easily, so visits from others should be a bit limited.*

*At this point, physical therapy is more routinely incorporated into the daily regimen. We have experienced therapists who know how far to push each patient. Exercise will increase circulation, help breathing, aid in keeping the lungs clear, increase leg strength, and make everyone feel better!*

*You will be expected to start learning about post-transplant care, including medications, PICC line care, blood pressure measurement, pulmonary function testing, pulse oximetry, signs and symptoms of infection and rejection, and general issues regarding lung transplantation. You may need to learn to measure blood sugar levels and how to give insulin.*

*We will provide for you a binder where you can write down numbers and results that we think are important, like blood pressure measurements, results from spirometry, blood tacrolimus levels, kidney function tests, and white blood cell count. This way, once you leave for your REAL home, you will know what is normal, and what isn’t normal, and can follow up with your doctor and the transplant team quickly when these change.*

#

# The Medications

*At this center, we most commonly use a triple-drug regimen to prevent rejection. We use tacrolimus, mycophenylate mofetil, and prednisone. Your child will also receive other medications initially, called induction agents, but these will generally be finished by 5 weeks after the transplant. The induction agent most commonly used is called anti-thymocyte globulin (ATG), but other biologics such as basilixumab or rituximab are often substituted, depending on the clinical situation.*

# ***Tacrolimus***

 *Tacrolimus (aka, FK506, Prograf) is an inhibitor of T-cells which are a specific subset of white blood cells. It stops them from being activated and from calling more in to the site of the lung. Thus, it causes the immune system not to ‘recognize’ the foreign lungs present in your child’s chest, and inhibits rejection from happening.*

*There is much variability of absorption among patients, so tacrolimus levels are monitored carefully by measuring whole blood levels. Tacrolimus is metabolized by the liver, so patients who have liver dysfunction have their levels monitored closely. There are several drug interactions that may increase or decrease tacrolimus levels and these may require more intensive monitoring. The table below lists some drugs that may affect tacrolimus blood levels.*

|  |  |
| --- | --- |
| Increase | Decrease |
| Diltiazem | Phenobarbital |
| Nicardipine | Phenytoin |
| Verapamil | Omeprazole |
| Erythromycin |  |
| Clarithromycin |  |
| Fluconazole |  |
| Itraconazole |  |
| Ketoconazole |  |
| Cimetidine |  |
| Tacrolimus |  |
| Metoclopramide |  |

*The target blood levels during the first month after lung transplant should be maintained between 11-14 ng/ml during the first 3 months, between 10-12 ng/ ml during months 3 – 6, between 8-10 ng/ml for the next 6 months, and 6 - 8 ng/ml thereafter.*

*Side Effects and Toxicities of tacrolimus. The most significant side effect is renal (kidney) toxicity. Other common side effects include hypertension, puffiness and overgrowth of the gums, excessive hair growth (forehead, face, mustache, back, arms, etc.), high blood sugar, high fat levels in the blood. Neurological side effects occur frequently, especially headaches, and other problems range from a mild tremor (shakiness of the hands) to seizures. Gastrointestinal complications include an upset stomach, nausea and diarrhea. Most side effects are dose related and improve with a reduction in dose.*

# ***Mycophenolate Mofetil (CellCept)***

*Mycophenylate suppress growth of the T- and B-lymphocyte populations. It has no kidney or liver toxicity, no effect on lipids and minimal drug interactions. The primary toxicities of mycophenolate mofetil are gastrointestinal and effects on the bone marrow production of red and white blood cells.*

# ***Corticosteroids***

*Corticosteroids are a mainstay of immunosuppression in lung transplantation, but the dose of corticosteroids is tapered to a low daily baseline in order to minimize the toxicities of chronic use.*

 *The side effects of corticosteroids are numerous and are associated with considerable morbidity. Corticosteroids have been associated with cushingoid features (acne, round facies, a fatty hump on the shoulders, mild obesity), weight gain, fluid retention, diabetes, stomach ulcers, high blood pressure, cataracts, emotional swings, osteoporosis (leading to fractures), poor wound healing and slow growth. The side effects associated with corticosteroids are clearly dose related and the dose is minimized as possible.*

# ***Sirolimus (Rapamycin)***

*The toxicities associated with sirolimus include low white blood cell count, low platelet count, rash, nausea, hyperlipidemia and mouth ulcers. It interacts with cyclosporine and tacrolimus, so doses of these drugs must all be carefully monitored if used together.*

# ***Cyclosporine***

*Cyclosporine is often used as an alternative to tacrolimus after lung transplantation. Cyclosporine is approximately 100 times less potent than tacrolimus. However, it is given in doses equivalent to tacrolimus to achieve adequate immune suppression.*

*The largest issue with cyclosporine is related to highly variable absorption from the intestines. Certain patient populations, including cystic fibrosis patients, African-Americans and diabetics, tend to absorb this agent erratically. We use a formulation of cyclosporine has been developed called Neoral® or Gengraf®. In general, absorption with Neoral® tends to be independent of interactions with food. The target blood levels during the first month after lung transplant should be maintained between 350-400 ng/ml during the first 3 months, between 300-350 ng/ ml during months 3 – 6, between 275-300 ng/ml for the next 6 months, and 250 – 300 ng/ml for the following 1 – 2 years.*

*Cyclosporine is metabolized by the liver. Use of certain other drugs can result in variable cyclosporine trough levels, similar to tacrolimus. CF patients should take cyclosporine and pancreatic enzyme replacement therapy at the same time.*

|  |  |
| --- | --- |
| ***Increase*** | ***Decrease*** |
| *Diltiazem* | *Phenytoin* |
| *Nicardipine* | *Phenobarbital* |
| *Verapamil* | *Rifabutin* |
| *Clotrimazole* | *Rifampin* |
| *Erythromycin* | *Omeprazole* |
| *Clarithromycin* |  |
| *Fluconazole* |  |
| *Itraconazole* |  |
| *Ketoconazole* |  |
| *Cimetidine* |  |
| *Cyclosporine* |  |
| *Metaclopramide* |  |

*Side Effects and Toxicities of cyclosporine. The most significant side effect is kidney toxicity, leading to hypertension. Other common side effects include puffiness and overgrowth of the gums, excessive hair growth (forehead, face, mustache, back, arms, etc.), high blood sugar, hypertriglyceridemia. Neurological side effects occur frequently, and range from a mild tremor (shakiness of the hands) to seizures. Gastrointestinal complications include an upset stomach, nausea and diarrhea. Most side effects are dose related and improve with a reduction in dose.*

# ***Other medications needed for lung transplant recipients***

*Your child may have received lungs from a donor who had certain viral infection, called CMV. If so, your child will receive an intravenous therapy for 34 days with a medicine called ganciclovir and with several doses of CytoGam, then will receive an oral form of gancyclovir called Valcyte for a period of 6 months. The reason for this is because it has been found that, at least in heart transplant recipients, if CMV disease activates in the first 6 months, the likelihood of rejection is greatly increased in the first year. With these medicines, we can control the activation of CMV and hopefully maximize post-transplant outcome and longevity.*

*Other medicines may be needed to help control the side effects of the immune suppressants, and therapy for high blood pressure and nausea is common.*

# Complications

# Infections

*Your child will be easily infected with any number of infections, viral, bacterial, and fungal. This is because the anti-rejection medications that are necessary to keep the new lungs from being rejected cause the immune system to be weak at fighting infection. They are at highest risk in the first 6 months, but as the dose of anti-rejection medication is being slowly decreased (under close supervision by your doctor), they are more capable of fighting infection in the 2nd and 3rd years.*

**If you notice ANY change or signs of illness (runny nose, fever, cough) you should call the transplant coordinator immediately.**

# Rejection

*There are four types of rejection that happen in lung transplantation:*

* *Hyperacute rejection (happens immediately after transplant).*
* *Acute rejection (most common in the first 6 – 12 months)*
* *Chronic airway rejection (aka, bronchiolitis obliterans)*
* *Chronic vascular (blood vessels) rejection*

# ***Hyperacute rejection***

*Hyperacute rejection is rare. But, if it occurs, can cause complete rejection of the lungs within 24 hours. Hyperacute rejection is caused by antibodies that were formed in the patient’s body sometime before the transplant takes place. Antibodies are immune proteins that are in your blood stream that serve to recognize and remove bacteria and infection and foreign cells. Antibodies are made by the immune system if your body is exposed to an infection. Patients can develop antibodies after receiving blood transfusions or during pregnancy. Therefore, the patients who have received blood transfusions, those who have had devices placed (patches, or homografts to vessels), multiple surgeries, previous infections are at the highest risk to develop antibodies to donors.*

*Your body makes antibodies, because antibodies protect us from infection. But, in the case of transplant, these antibodies (called anti-HLA antibodies) can recognize the proteins on the donor’s lungs. The antibodies activate the immune system when they attach to the ‘foreign’ proteins of the donor lung. This results in a rejection episode and causes injury to the transplanted lungs. Injury from the immune system can lead to worse lung function and decreased oxygen levels and even permanent damage.*

*We monitor this by drawing blood every 60 – 90 days for a test called HLA PRA, to test for the presence of anti-HLA antibodies that might have been formed. If there are indications for hyperacute rejection, those donors will not be accepted for your child. In some cases, with ‘weaker’ reactions seen on the test, there are certain things that can be done to try to remove the anti-HLA antibodies from your child’s blood. Your child may have to receive IV gamma globulin to counteract that. If these treatments are ineffective, your child may have to undergo plasmapheresis, to remove those antibodies from the bloodstream during and after the transplant. Even after receiving treatment, your child could remain at high risk for hyperacute rejection after transplant, then your child may have to undergo ongoing plasmapheresis treatments to prevent this from becoming a long-term problem.*

#

# ***Acute Cellular Rejection***

*Acute rejection occurs when immune system cells called T-lymphocytes identify foreign proteins on the surface of cells in the transplanted lung and cause injury to those cells. This is a normal function of the immune system, and is important as a response to control the growth of tumors and viral infections. But, in transplant recipients, this must be controlled carefully with the use of immune suppressing medicines (tacrolimus (Prograf), mycophenylate mofetil (CellCept),and prednisone).*

*Acute rejection most often occurs in the first 6 months and is usually detected at a mild stage, since there is increased surveillance with bronchoscopy and biopsy during the first 6 months after transplant. Surveillance biopsies are done every 2-4 weeks after transplant for the first 8 weeks, at the 3rd and 6th month, then again at 12 months, and annually thereafter. Biopsies might be done sooner or more frequently of there is evidence of acute rejection happening.*

*There are grades of acute rejection, and the scale depends on how far the lymphocytes extend into the tissue surrounding the blood vessels. Acute rejection occurs when the T-lymphocytes become activated. The T-lymphs enter the new lungs by way of the blood vessels. The first sign that acute rejection has occurred is when the pathologist sees many of them surrounding the blood vessels on the biopsy specimen obtained at the time of bronchoscopy and transbronchial biopsy. (A0 – none; A1 – minimal; A2 – mild; A3 – moderate; A4 – severe).*

***How will you know if your child is experiencing rejection?***

*Acute rejection can occur with or without outward symptoms. If symptoms are present, they are similar to a lung infection, and include:*

* *Fever, cough, difficulty breathing.*
* *Decrease in pulmonary function tests (FVC and FEV1).*
* *Elevated white blood cell count (WBC).*
* *Abnormal chest x-ray (pleural effusion or pneumonia-like changes, or both).*

***How is acute rejection treated?***

*Most episodes of acute rejection respond to treatment with high doses of steroids and will not have a significant impact on your child’s lung function. Grade A2 or worse is initially treated with a “pulse” of Solumedrol (IV steroid) once a day for 3 days.*

*Two to four weeks after completing treatment, we will repeat the bronchoscopy and biopsy to make sure the rejection is resolved.*

*If the rejection is still present on the follow-up biopsy, and it is not improved, we will treat with a special IV antibody called basilixumab (an anti-lymphocyte antibody that blocks T-lymphocyte activation). We may also change the immunosuppressant therapy to different medication such as sirolimus.*

*Most patients have at least one episode of acute rejection, though the risk may be lower in children less than 1 year of age. In most patients, the acute rejection resolves after treatment with Solumedrol.*

*It is important to remember that rejection is a continuous threat even beyond the first 6 months, especially for transplanted lungs as opposed to other organs. Your child will take immune suppressants (tacrolimus, mycophenylate, and prednisone) for the rest of his or her life. If blood levels of the immune suppressing drugs are too low, rejection can occur. If rejection is chronic, i.e., long-standing, the chances of reversing the rejection process are low, and mortality (death) is high since the lungs cannot function normally.*

#

# ***Bronchiolitis Obliterans***

*Bronchiolits obliterans is the most important disease that limits long term survival after lung transplantation. It is also the most common complication occurring more than a year after lung transplant.*

*There are different names for bronchiolitis obliterans: BOS, chronic airway rejection, chronic lung rejection. The name refers to the changes of lung function testing and xrays, and sometimes is found on biopsy. Bronchioles are the smallest airways in the lungs and these are the parts damaged in BOS. As damage progresses, scar forms. When the disease is advanced, the airways become completely obliterated, there is no longer a passageway for air. The symptoms of BOS are noted by shortness of breath and low oxygen saturation levels. There are multiple causes for this, but the exact reason for it has not been discovered. It is thought that prolonged ischemic time (time with the donor lungs out of the body at the time of the transplant surgery), episodes of acute rejection or antibody-mediated rejection, or the occurrence of chronic infections may contribute. CMV infection may be one of the more common causes. Children who receive their transplant before the age of 3 years appear to be at lower risk.*

***How do you know if your child might be developing OB?***

*Patients who develop OB may have chest cold symptoms or initially may have no symptoms at all. The most useful EARLY indicator of OB is a drop in lung function (FEV1) that is not otherwise explained.*

*Symptoms of more severe OB include:*

* *Dry cough or productive cough that is not related to an infection.*
* *A new onset of shortness of breath with or without exercise.*
* *A decrease in lung function (FEV1) that is otherwise unexplained.*
* *A decrease in oxygen saturations will eventually occur but is a late sign.*

*The diagnosis of BOS is difficult, and usually requires more than one test. If we see a drop in your child’s FEV1, we will obtain a V/Q (ventilation/perfusion) scan and a CT scan. If these show signs suspicious of OB, an open lung biopsy may be necessary to confirm the diagnosis. (We ask the surgeons to obtain a larger portion of the lung by ‘open lung biopsy’).*

 ***How does BOS affect your child?***

*There are 3 patterns of progression of lung dysfunction in OB (in order of most to least common):*

* *Slow onset and slow progression.*
* *Rapid onset with initial decline in lung function and then stabilization of lung function for months to years.*
* *Rapid onset, rapid decline.*

***How is BOS treated?***

*BOS cannot be cured, but the progression of lung damage can be halted or slowed. The treatment is variable, and depends on previous complications or infections that occurred after transplant. Usually, the first step is treatment with basilixumab, IVIG, and plasmapheresis, or other antibody ‘biologics’ that target different T- or B-cell populations. We also optimize the immune suppression medicines.*

#

# ***Post-Transplant Lymphoproliferative Disease (PTLD)***

*PTLD is a disease that all transplant patients are at risk of developing because of the immunosuppressed state that is required to maintain the graft in good function and avoid rejection and OB. PTLD is a form of cancer that occurs most often in children who were not exposed to the Epstein-Barr Virus (EBV) prior to transplantation, but who are exposed after the transplant. EBV is the virus that causes “mono”, the kissing disease. It can develop in children who were previously infected with EBV or the exposure after transplant happens if the donor of the lungs had been previously infected, or it can occur from exposure to EBV in other people. Someone who has been infected in the past with EBV will always test positive for the virus. Usually, the virus lies dormant (sleeps) in the B-lymphocyte cells (B-cells) of the immune system. The EBV can reactivate (come out of dormancy) because the child is immune-suppressed. When this happens, B-lymphocytes (B cells) will grow. In this setting, the B cells grow so rapidly, that they act like a cancer tumor.*

*PTLD occurs in about 15% of pediatric lung transplant recipients. It most commonly occurs in the first two to three months following transplantation but may occur many years after transplant. Some patients do not have symptoms at all and the tumor is found during a routine physical examination. Other patients have flu-like symptoms, and some patient have problems associated with the body part that the tumor forms in (liver problems, cough, etc).*

*The prognosis depends on the amount and location of tumor formation and the disease’s response to treatment. In some of the cases, PTLD is fatal.*

*There are several types of treatment options for PTLD. Most often, the doses of your child’s immunosuppressive medicines will be decreased, and treatment with chemotherapy (like cancer patients) will likely be required. The doctors who treat cancer will be asked to help manage the PTLD if chemotherapy is required to treat it.*

Immune Suppression

*Since the donor lungs come from people unrelated to your child, your child’s immune system will try to get those lungs out of his body. That is what a normal immune system does. If this happens, we call this process rejection. If the lungs are rejected, your child will not survive. Rejection destroys the lung tissue, and can occur very rapidly or can proceed slowly, even if your child is taking the medication, if the blood levels or the anti-rejection (immune suppressants) medications are not high enough. Rejection can even happen if your child is taking the mediations properly.*

*Acute rejection is most common in the first 6 months after transplant, and for this reason, your child will be very closely monitored. The schedule for testing is discussed in the next section. What is very important to understand is that all post-transplant patients must learn to take their immune-suppressants by mouth, even if they already have a G-tube in place. This is because the medication doses are very specific, and the dosage is changed based on blood serum levels. These medications ‘stick’ to the G-tube, and do not get absorbed into the blood stream in a reliable way. The medicines must be taken orally, either in liquid or pill form.*

# The First Three Months

*Once your child no longer requires oxygen, and all chest tubes are out, and your child is up and walking and eating well, she/he will be discharged to the Ronald McDonald House. The Ronald McDonald House is just down the street from LPCH, and there is a shuttle bus that can take you back and forth. You will be staying in the building for ‘immunosuppressed’ patients and their families. Both parents can stay, but other siblings cannot, though they can visit. This is because they might transmit infections to other immune- suppressed patients in the building. You will be required to stay for about 3 months, even if your home is very close to the hospital. This time immediately post-transplant is the most critical and exposure to infections and other things that can trigger rejection must be minimized.*

*It will be a huge adjustment to leave the hospital. Most people look forward to leaving the hospital, but actual discharge can be met with mixed emotions. The medication schedules, blood pressure monitoring, etc. may seem overwhelming. Prior to your departure, we will go over your medications and review any side effects that your child might experience. You can ask the transplant team any questions before and after leaving the hospital. There will be as much time as you need to prepare you for discharge.*

*Your child might require daily IV medications that will require visits to the Short Stay Unit (SSU). Your child’s blood levels of tacrolimus,r white blood cell count, or kidney function may need to be checked several times a week. This is done either in the SSU, where they can draw the blood from the Broviac or Mediport, or at the Outpatient Laboratory.*

*You will be seen in clinic each week. For each visit, we will obtain blood tests, chest x-rays and spirometry (breathing tests) to make sure that there is no evidence for rejection or infection.*

*It’s important to remember that everyone recovers from surgery at a different pace. It is normal to have good days, as well as some not so good days as your child recovers. Your child’s body is going through many adjustments as he recovers from the surgery, and as he gets used to the new medications. He will be slowly resuming regular activities. Some transplant recipients learn how to do things that they never did before! The challenge is to help your child achieve whatever his dreams are.*

# Instructions For Discharge

*The child should not lift anything greater than 10 pounds for six weeks after surgery and not participate in strenuous activity for six weeks. We will have you follow up in the Physical Therapy twice a week to help with the proper types of exercise to accomplish.*

*Check your child’s chest incision every day. If there is unusual redness or swelling, pus or drainage, or pain, contact the transplant nurse immediately. Clean the incision daily with warm water and soap.*

*Check the PICC or Mediport site every day. If there is any redness, swelling, pus, drainage, or pain, contact the transplant nurse immediately.*

**Call the transplant nurse, or on call physician immediately, for any of the following:**

1. Fever over 99.6oF.
2. Flu-like symptoms (achiness, nausea, vomiting, runny nose, etc).
3. Cough or shortness of breath
4. Blood in the stool
5. Nausea, vomiting, or diarrhea
6. Chills
7. Redness, swelling, drainage, pus, or pain at the incision or central line site.

# In The First Months Post-Transplant, You Will Be Busy...

|  |  |
| --- | --- |
|  First Month  | Second and third Months |
| * Weekly clinic appointment
 | * Clinic appointment every 2 wks
 |
| * Chest x-ray and spirometry twice a week
 | * Chest x-ray and spirometry every week
 |
| * Blood tests weekly (drug levels, electrolytes, CBC)
 | * Blood tests every 2 weeks
 |
| * Pulmonary Rehabilitation Program 3 times a week
 | * Pulmonary Rehab follow-up as recommended
 |
| * Surveillance bronchoscopy at 2 and 4 weeks post-op.
 | * Surveillance bronchoscopy at 6, 8, and 12 weeks post-op.
 |

MEDICATION LIST

|  |  |  |
| --- | --- | --- |
| Name of Drug | How often taken | **Target Blood Level** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**BLOOD PRESSURE CHART**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date | BP | Date | BP | Date | BP |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

# Phone Numbers

**Transplant Nurse Coordinator**

Jennifer Shek, RN 650-725-3810 FAX 650-736-8912

Transplant Physicians

Dr. Carol Conrad, Director Call pre- or

Dr. Carlos Milla post-transplant

Dr. David Cornfield nurse, or operator if after hours

Hospital Operator 650-497-8000

 650-723-4000

Tamzen Hull, MSW 650-725-9626

# Frequently Asked Questions

**Is my child cured after getting the transplant?**

It will surely seem like it. Your child will very likely feel much more normal than they ever have before. We encourage your family to live as normal a life as possible. This means going to a regular school, participating in social and group activities, playing sports, traveling, dating (yikes), mountain climbing, getting married, starting a new career.

But, your child is not really ‘cured’. By getting a lung transplant, your child received the wonderful opportunity to live several years longer than he or she would have without a transplant. But she still must take medications every day for the rest of her life to prevent rejection. And there are many side effects of the medications that must be combated. So, in effect, they have ‘traded’ one disease for another.

Children who were transplanted because they had cystic fibrosis still have cystic fibrosis. This means your child will continue to need treatment and medications to help with food absorption, enzymes are necessary (which must also be used with cyclosporine), extra vitamins are necessary, and the likelihood of developing insulin-dependant diabetes is higher, since they will be taking prednisone.

The lungs of a CF patient won’t ‘get CF’ again, since the lungs are genetically normal, but, they can be infected with the bacteria that your child still has present growing in the nose, sinuses, and upper trachea.

**Why do we have to live at the Ronald McDonald house for so long – I live 10 miles away!**

Your child will have a very low resistance to ANY kind of infection because of the immune-suppressant medications that she is taking to prevent rejection. The You will be staying in a special part of the Ronald McDonald house that is special for ‘immune-suppressed’ patients. Most types of visitors are restricted from visiting it, and thus, we can provide a more protected place for your child to live during the time when they are most susceptible to getting very ill, even from a simple cold. Once we are assured that your child is safe and doesn’t need so much isolation from exposure to infections, that’s when you will be discharged to your own home.

**When can my child go back to school?**

Generally speaking, they can return to school 6 months after they have had their transplant. They are most immune-suppressed in those three months, thus are most susceptible to infection from viruses and other infections kids can pass to each other at school.

**When can we travel?**

The same idea is true as for school, but it may be best to wait until 6 months. Airplanes often re-circulate the air in the cabin, and this increases the likelihood of getting an infection, even higher than exposure that occurs in the schoolyard.