

LONG-TERM COMPLICATIONS

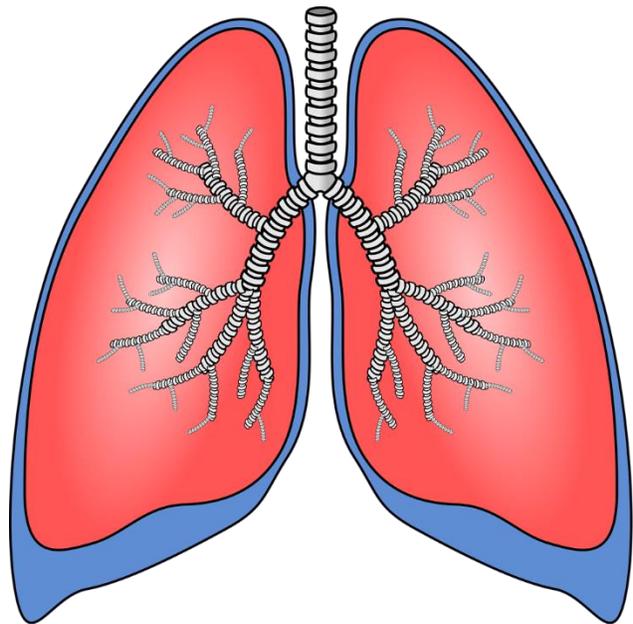
“Rejection” is a word that someone who has had a lung transplant never wants to hear. It sounds scary, and it can be, because you want your body to accept your new lung(s) completely. When you hear the word “rejection,” you know that your body is having a problem accepting your new lung(s) as its own. Understanding acute and chronic rejection will allow you to have an informed discussion with your doctor about treatment options.

DETECTING REJECTION

As a lung transplant recipient, you will have scheduled bronchoscopies following your transplant. During this procedure, a number of small pieces of your lung are snipped to determine whether acute rejection or other inflammation is present. A rinsing of your lungs is also done to determine if there is any infection in the transplanted lung(s). You will have several surveillance bronchoscopies performed during your first 2 years following transplant. These are done to inspect your airways and look for signs of infection and/or rejection. You may have additional bronchoscopies performed if rejection or infection is suspected (or if other problems are present, such as a narrowing of your airway, called stenosis).

ACUTE CELLULAR REJECTION (T-LYMPHOCYTE REJECTION)

Around 40 percent of lung transplant recipients will experience an episode of acute rejection within the first year. Some people may notice increased shortness of breath, cough, or a drop in their PFT's, but others may not have any symptoms of rejection. For this reason, your transplant team will tell you to call the office if your home PFT's change by more than 10% over a 3 day period. If you are found to have acute rejection, treatment for acute rejection usually includes three daily doses of intravenous steroids, followed by an oral prednisone taper over the next few days to weeks until you are back down to your home dose. Not all treatment needs to be done in the hospital. You will need to take extra precautions to avoid exposing yourself to infections when you are on increased steroids, and may need to watch your blood sugars more carefully. Follow-up bronchoscopies may be done to determine whether the rejection is fully cleared. For most people, PROMPT diagnosis and treatment of acute rejection is quite effective, and lung function typically returns back to normal. However, if there is ongoing rejection, your doctors may consider other treatment options.



CHRONIC REJECTION

Also known as *Bronchiolitis Obliterans Syndrome (BOS)* or *Chronic Lung Allograft Dysfunction (CLAD)*. The lungs have higher rates of rejection compared to other transplanted organs, as lungs tend to have a stronger immune response than other organs. The most common long-term complication of lung transplant is chronic rejection. Chronic rejection is present in approximately half of all recipients within five years of the transplant. The course varies for each transplant recipient. **Some patients may have mild chronic rejection** without a major change in symptoms and little reduction in the life of your transplanted lungs, while **others can have a rapid progressive course** that causes the lungs to fail. Diagnosis of chronic rejection is usually based on declining PFT's (FEV1) and is usually due to scar tissue in the small airways of the lungs.

Risk factors for chronic rejection include, but are not limited to:

- Gastro-esophageal reflux disease (GERD)
- Ongoing acute rejection and/or antibody-mediated rejection episodes
- Missing anti-rejection treatments and medication doses
- Early lung injury, known as primary lung graft dysfunction (PGD)
- Fungal, bacterial, and viral infections

Chronic rejection can also occur without any known risk factors. While **there are no proven treatments to reverse chronic rejection**, your lung transplant team will work very closely with you to promptly identify and treat any conditions that could be a risk factor for chronic rejection. Prompt treatment can reduce your chances of developing the condition. Examples of this include, treating any infections, correcting reflux, treating antibody-mediated rejection. **Treatments that may help limit the progression of chronic rejection include:**

- Changing the dose of your anti-rejection medications
- Adding additional medications to your immunosuppressant regimen such as mycophenolate, everolimus, or azithromycin
- Photopheresis treatments

Patients often ask about re-transplant if they develop severe chronic rejection. This option is considered on a limited, case-by-case basis depending on the patients' health at the time of the situation. As a patient, you can do your part to reduce the risk of chronic rejection by taking the best care of yourself, taking your medications as prescribed, and reporting any symptoms to your transplant team.

ANTIBODY MEDIATED-REJECTION (B-LYMPHOCYTE REJECTION)

Antibody-mediated rejection is another way your body's immune system may react to your donor lung(s). This form of rejection **is caused by antibodies that target your donor lung(s)**. These antibodies can be present before transplant (especially if you have had a previous pregnancy, transplant, or blood transfusion) or can develop after transplant. We will screen for this with a blood test on the same schedule as your bronchoscopy and if you have any unexplained decline in lung function. The blood test to check for antibody-mediated rejection can **ONLY** be performed at Johns Hopkins Outpatient Center

Express Testing. Treatments for antibody-mediated rejection will be different than those used for acute cellular rejection. **These treatments typically include some combination of the following** depending on the severity of the condition.

- Intravenous Immunoglobulin, a recurring IV treatment to bind donor specific antibodies (IVIg)
 - Can be done as an outpatient or in the hospital
- Rituximab, a one-time long term treatment to reduce antibody producing cells
 - Can be done as an outpatient or in the hospital
- Plasmapheresis to remove antibodies
 - Requires a hospital admission for 10-14 days

Rejection Fast Facts:		
Cellular Rejection	VS.	Antibody-Mediated Rejection (AMR)
T-cells		B-cells
Diagnosed with bronchoscopy		Diagnosed with blood test
Acute Rejection – easily responds to treatment		Antibody-mediated rejection, also known as humoral
Chronic Rejection – slow decrease in lung function with time		Donor specific antibody test

Infection Risks with Transplantation

Infections are common after transplant. The anti-rejection drugs that help keep your donor lung(s) working after transplant reduce the body's ability to fight off infections. Thus, many exposures that would not have been harmful prior to transplant can cause serious infections after your transplant.

Bacteria, viruses, fungus, or other organisms can all cause infections which can affect your immediate health or lead to chronic rejection if left untreated. Over the years, we have developed precautions to greatly reduce the risk of infections, but some risk will always remain. We ask that you follow our recommendations closely so that you can remain as healthy as possible.

Don't wait to call. Because you are on anti-rejection medications you will not feel as sick as you did before transplant, or as sick as your family members.

We will work with you to minimize the risk of infections by:

- Giving preventive anti-infective medications following transplant
- Stopping or switching anti-infective medications if you are having side effects
- Asking you to call us EARLY with any symptoms of infections
- Monitoring and testing patients closely following transplant
- Following the Safe Strategies for Living (*see page 53*) to protect yourself and your family
- Consulting with transplant infectious disease experts if needed for complex situations

Call the transplant office if you have:

Fever above 100°
Chills
Runny or stuffy nose
Headache

Sore throat
New or change in Cough
Body aches
Diarrhea and vomiting



Emergency Warning Signs:

If you have any of the following you please notify us and go to the hospital

Increasing Difficulty Breathing Pain or pressure in the chest or abdomen
Sudden dizziness Confusion
Severe or persistent vomiting or flu like symptoms that improve but return with fever

VIRUSES

Respiratory viruses such as the flu and colds occur throughout the year, but are most common in the fall and winter. Our transplant team takes viruses very seriously as certain viruses that would have been considered mild colds prior to transplant, can lead to chronic rejection if untreated. Wearing a mask outside the home during cold and flu season can help protect you from harmful viral infections. If someone in your household has cold symptoms or a positive flu or respiratory syncytial virus (RSV) test, please let us know as you may also need to be treated with a preventive medication. You and household members should also get the flu vaccine (injection only) when available.

****If you are having ANY signs or symptoms of a cold, please call the Transplant Center IMMEDIATELY so that we can diagnose and treat as needed.**

If you call with sick symptoms, the transplant team will typically ask you to go to Outpatient Center for the following tests:

- ✓ PFT
- ✓ Respiratory Viral Swab
- ✓ Chest X-ray

****Please call the transplant office after the tests are completed to determine the next steps.****

Cytomegalovirus (CMV) is a common viral infection that most patients and donors have been exposed to at some point. When you have a healthy immune system, the virus remains present, but silent in your body. After transplant, if your immune system cannot control the virus it can become active in your blood and cause a range of mild or severe symptoms including **drop in home PFTs, body aches, fevers, pneumonia, stomach upset or diarrhea**. If you or your donor had a positive blood test for the CMV virus, we prescribe anti-viral medications for several months until you are on lower doses of anti-rejection medicine. CMV infection may occur in some patients after the preventative treatment is stopped, but you will be screened for this virus with your routine bloodwork so that we can catch and treat any active infection promptly. CMV infection after lung transplant can increase the risk for chronic rejection. If you experience any of the above symptoms, please tell your transplant team **immediately**.

YOUR CMV STATUS
DONOR _____ / RECIPIENT _____

YOUR EBV STATUS
DONOR _____ / RECIPIENT _____

Epstein-Barr virus (EBV) is a virus to which most donors and patients have been exposed, and, similar to CMV, it remains silent if your immune system can control it. New infections can cause mononucleosis “mono”, but this is fairly rare after transplant. More seriously but also very rarely, it can cause a condition called Post-Transplant Lymphoproliferative Disease (PTLD) which is a type of blood cancer. You will be monitored for EBV after transplant, through routine bloodwork depending on you and your donors’ prior history of exposure. If there is any concern for PTLD, you will have additional tests performed and may need further treatments for the condition.

BACTERIAL INFECTIONS

Donors and recipients may have bacteria in their lungs at the time of transplant, or may be exposed to them at later time points. Some bacteria are normal in the respiratory system, while others can lead to pneumonia if left untreated. We will get routine cultures from sputum or during your bronchoscopy to monitor for any bacterial infections throughout the first two years, and if you have a change in your lung function or breathing that raises concern for infection. You may be on antibiotics immediately following your transplant surgery; these antibiotics will be adjusted according to culture test results. Long term, you will be on at least one preventive antibiotic. A preventive antibiotic is not used to treat an active infection; instead it is used to prevent infections from developing when your immune system is low. You may also intermittently need antibiotics by pill, inhaled, through sinuses, or through IV line to treat new infections or pneumonia, depending on the culture results from your bronchoscopies and other tests.

MOLD INFECTIONS

Mold and fungus exposure is common after transplant, especially in the Mid-Atlantic region where we have a fair amount of moisture and rain year-round. Lung transplant recipients are particularly vulnerable to invasive mold that can cause pneumonia, airway complications and chronic rejection if undiagnosed or untreated. To reduce exposure to mold, please follow the guidelines for water safety that are detailed in the Strategies for Safe Living section (see *page 53*). Common exposures can be with gardening/farming in dirt, exposure to construction sites, and water damage in homes. Mold infections can often occur without any symptoms, or may present with shortness of breath, wheezing or new cough. We will monitor for mold infections with each bronchoscopy and treat you with antifungal medication if results show exposure to a mold or fungus. When you are on antifungal medications, you will need bloodwork to make sure you are on a correct dose. Additionally, antifungal medications interact with tacrolimus and cyclosporine, making blood work important to monitor your lab results.

OTHER NON-INFECTIOUS CONDITIONS

Diabetes

Both tacrolimus and prednisone can cause your blood sugar levels to rise. Although, you may not have had diabetes before transplant, you may have to monitor blood sugars and/or take insulin to control your blood sugars post-transplant. If you had diabetes before transplant, these medications will make it harder to control blood sugars. Managing blood sugars helps prevent further complications, such as kidney, eye, or cardiovascular diseases. Elevated blood sugars can also lead to increased risk of infection, and makes them more difficult to treat.

General guidelines for managing blood sugars:

1. Exercise regularly
2. Have a consistent intake of carbohydrates
3. Limiting intake of sugar sweetened beverages
4. Choose higher fiber foods
5. Maintain a healthy body weight

Carbohydrate counting is one meal-planning tool that can help you manage blood sugars. It provides flexibility and more options when planning meals. Carb counting can be used for those taking insulin and those who are being managed with diet. With the help of a registered dietitian, you will learn what foods contain carbohydrates, and develop an individualized plan to help you manage your blood sugars. If you take insulin, carbohydrate counting allows you to match the number of carbohydrates consumed during a meal to your dose of insulin.

Online Resources to Make Carb Counting Easier

MyFitnessPal

<https://www.myfitnesspal.com/>

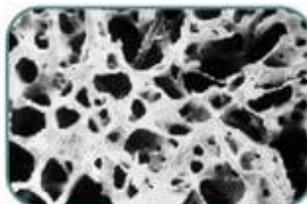
Fooducate

<https://www.fooducate.com/>

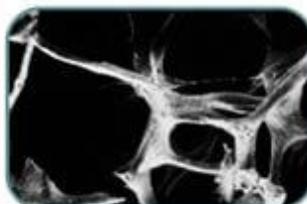
BettrLife

<https://www.bettrlife.com/>

Osteoporosis



Normal Bone



Osteoporotic Bone

Osteoporosis is a condition where the structure and strength of the bones are weakened. This may increase your risk of fractures. Several factors that contribute to osteoporosis include age, diet, and menopause. Transplant patients have an increased risk for osteoporosis because prednisone can weaken the bones with long-term use. A bone density test is done before your transplant to provide a baseline assessment. Repeat scans done after your transplant can be compared to look for changes. **You can help keep bones strong**

by eating a diet that contains at least 1000 mg calcium/day and doing daily weight bearing exercise such as walking, or strength training. Calcium pills and vitamin D supplements may be used after transplant to supplement diet. Stronger bone building medications may also be prescribed by your PCP, transplant team or a specialist.

Coronary Artery Disease and Risk factors for Heart Disease

It is important to take care of your heart as well as your lungs after lung transplantation. Eating foods low in sodium, cholesterol, and sugars will help reduce your risk of developing high cholesterol and high blood pressure, which can lead to the development of heart disease. Maintaining a healthy weight and exercising also helps to reduce your risk. You should **never** smoke, and minimize the amount of alcohol you drink as recommended by the transplant team.



Hypertension (High Blood Pressure)

You will be asked to keep track of your blood pressure once you go home. High blood pressure is the most common complication following transplant. It is a side effect of the anti-rejection medications, and may have existed prior to transplant. Extra salt in your diet will cause you to retain extra water and your blood pressure will rise. You can help control your blood pressure by watching your weight, exercising, and avoiding high sodium foods, such as canned foods, food prepared outside of home, and deli meats. **Your TOTAL sodium in food should be less than 1500 mg/day (¾ teaspoon).** Left untreated high blood pressure can damage your heart, kidneys, and the blood vessels in your brain. If you develop high blood pressure, you may be given medications to lower your pressure.

High Cholesterol

High cholesterol levels may occur after transplant. If you had high cholesterol before the transplant, these levels may become higher after transplant due to the side effects of prednisone and cyclosporine/tacrolimus. Other factors such as heredity, diet, and other medical conditions such as diabetes can also affect your cholesterol. Your cholesterol levels will be checked after transplant. If they are high, you may be asked to reduce foods in your diet that are high in cholesterol, lose weight and exercise. If your cholesterol level remains high after diet and exercise, you may need medications to help lower cholesterol levels.

Cancer Screening

Transplant recipients have an increased risk of developing certain types of cancer because your low immune system makes it harder for your body to fight off early cancer cells. Generally, the earlier any cancer is detected, the easier it is to treat. Therefore, it is important to follow screening recommendations for cancer and work with your primary care team so that they can treat any concerning findings early. Sunscreen, skin protection and healthy diets are also important preventive measures to reduce the risk of cancer. It is advised that you wear, at least, **SPF 30 at all times**. When outside in sunlight, please cover all skin as much as possible. Light layers and hats are recommended. Please reapply sunscreen every two hours, or after being in water.

Screening Guidelines will be individualized for your health and risk but general recommendations are as follows.

Condition	Test	Who needs it	How often
Skin Cancer	Dermatology visit	Everyone post-transplant	Every 1 year
Colon Cancer	Colon Cancer	Adults over age 45; over 35 for cystic fibrosis patients	Every 3-10 years
Prostate Cancer	PSA blood test	Men over age 50	Personalized
Breast Cancer	Mammogram	Women over age 40	Every 1-2 years
Cervical Cancer	Pap Smear	Women over age 18	Every 1-3 years
Lung Cancer	CT scan	All transplant recipients	Yearly
Post-Transplant Lymphoproliferative Disorder (PTLD)	Blood test	Transplant recipients with EBV exposure	Routine lab work

Kidney and liver dysfunction

The immunosuppressive medications used after transplant are cleared out of the body through both the liver and kidneys. Several critical transplant medications can cause stress on kidneys and liver. For this reason, we examine other organ function closely via blood work before and after transplant, ask about side effects, and adjust medication doses if needed. To protect your kidneys and liver, we ask you to avoid other medications or supplements which can impair their function. If we notice any injury, we may refer you to a nephrologist or hepatologist. Patients who had “borderline” normal kidney function prior to transplant may experience long-term kidney damage after transplant. Rarely, patients who have progression of kidney damage may need dialysis or a kidney transplant.

DO NOT TAKE THE FOLLOWING:

- Pain medication in the NSAID family (Ibuprofen, Naproxen)
- IV contrast for CT scan – unless transplant doctor approves; oral dye is okay
- Foods/substances that can increase tacrolimus/cyclosporine levels
- Limit alcohol intake



DIGESTIVE HEALTH

Your digestive system and its effect on lung health:

Gastroesophageal Reflux Disease (GERD), also known as reflux or heartburn, is a condition caused by the backflow of digestive acids from the stomach and small bowels into the esophagus. This condition affects up to 50% of patients after transplant. Reflux can cause irritation to the esophageal lining and spill acid or stomach contents into the lung airways, even if you do not have any signs or symptoms of reflux. Patients with altered digestion may experience, heartburn, early fullness, bloating, or difficulty swallowing. They may also have none of the above symptoms. More importantly, GERD can affect the health of your transplanted lungs and cause cough, hoarseness, or even chronic rejection of the lung(s). For this reason, we will examine your digestive system very closely to look for reflux, or other disorders of the digestive tract.

What can you do to minimize reflux into your lungs?

It is very important that you take the following steps in order to reduce GERD symptoms:

- ✓ Eat at least 3-5 small, balanced meals a day, and allow at least a three-hour period between eating and lying down.
- ✓ If you are more than 10 pounds overweight, begin a plan to lose weight.
- ✓ At bedtime, raise the head of the bed six inches on bed blocks or use some kind of wedge support for your upper body (head of bed to 30°).
- ✓ **Do NOT smoke.**
- ✓ Reduce intake of coffee, caffeine and alcohol.
- ✓ Avoid high-fat foods and increase protein-rich foods.
- ✓ Reduce intake of the following: tomato products, citrus juices and fruits, peppers, onions, garlic, mint, cinnamon and chocolate.

How will the doctors examine my digestive system?

After transplant we will refer you to our gastroenterologist to better understand your reflux, they may recommend the following:

1. *Esophagram* is a swallowing test where you swallow oral contrast and a video x-ray of your swallowing muscles is done.

2. A pH Probe and manometry test to measure the acid in your stomach and examine your esophagus. This is a two-day test where a very thin tube is placed into your stomach and measures swallowing and acid content while you are eating and drinking.
3. A gastric emptying scan is a 4 hour test to measure how quickly your stomach digests food.

How are digestive disorders treated?

- All patients will be on anti-reflux medications to reduce stomach acid. However this does not fully prevent stomach content from coming into your lungs if you have reflux.
- Your team may recommend surgical correction or tightening of the valve between the stomach and esophagus to reduce symptoms and protect the transplanted lung(s) from long-term damage. This is called an anti-reflux surgery (ARS) or fundoplication.
- Your team may use medications to speed digestion if you are having reflux due to slow stomach emptying.
- In rare cases, you may be asked to have a temporary feeding tube if you have severe reflux or a poorly functioning esophagus, and there is concern that your lung is becoming injured. We will usually advise you of this possibility if we see something of concern on your pre-transplant testing, but occasionally problems arise that were not noted before transplant.

Bowel Movements

Your bowel habits may change after transplant particularly with some of the anti-rejection medications, which can cause softer, more frequent stools and with pain medication, which can cause constipation. Soft, non-liquid stools which are regular are usually not worrisome.

However please let your transplant team know if you have:

1. Sudden diarrhea
 - ✓ We would look for infections, and you may need medications to treat this
2. Signs of blockages, constipation or obstruction
 - ✓ Decrease in the amount or frequency of bowel movements
 - ✓ Painful stomach aches or cramping
 - ✓ Abdominal bloating
 - ✓ Feeling of fullness or inability to eat
 - ✓ Nausea and/or vomiting
 - ✓ Liquid diarrhea (liquid stool can be going around the obstruction)

Call the transplant office if you are having symptoms of a bowel obstruction or new diarrhea

Cystic Fibrosis patients may develop distal intestinal obstruction syndrome (DIOS), which involves a partial or complete intestinal blockage by thickened or sticky stool. This can be triggered by:

- ✓ Missing enzymes or incorrect dosage
- ✓ Dehydration: drink 8-10 glasses of water daily
- ✓ Receiving oral contrast – a small amount is given during swallow tests
- ✓ Constipation due to narcotic pain meds

Prevention of Obstructions:

- ✓ Taking enzymes regularly
- ✓ Staying well hydrated. Drink 8-10 glasses of water daily, drink more if outside in the heat or exercising
- ✓ Taking Miralax, Go-lytely, or other stool softener as preventative therapy

HEALTH MAINTENANCE

Primary Care Provider

- It is important to maintain a relationship with your pre-existing primary care provider (PCP).
- Your PCP can perform routine physical exams, and give preventative healthcare. If they are comfortable, they can manage conditions such as blood pressure and diabetes medications in coordination with the transplant team.
- Please always contact your lung transplant team prior to starting any new medication prescribed by your PCP or other doctors. Your transplant team can make sure that the new medication will not interact with your transplant meds.

Routine Screening & Preventative Requirements

- Dental Exams (every 6 months)
 - Notify coordinator, primary care, or dentist to order pre-antibiotics
 - Antibiotics are taken 30-60 minutes prior to every dental appointment
- Eye Exams – Recommended due to prednisone use, or if you have diabetes or sarcoidosis
- Bone Density Scans – Every 1-2 years to monitor for osteoporosis
- Annual blood work and urine testing

Preventive Cancer Screening

Transplant recipients have an increased risk of developing certain types of cancer because your weakened immune system makes it harder for your body to fight off early cancer cells. You should wear sunscreen, get routine mammograms, colonoscopies, pap smears as needed for your age so that we can take care of issues before they become serious concerns. A more detailed list is in the cancer screening section (see *page 69*).

Immunizations/Vaccinations

Influenza injection	Every fall
Strep Pneumonia vaccine (Pneumococcal-23)	Every 5 years
Strep Pneumonia “booster” (PREVAR 13)	Once
Tetanus and pertussis (TDAP)	Once
Tetanus booster (Td)	Every 10 years
Cervical cancer vaccine (HPV)	Adults under age 26

You should **NOT** have any vaccines that contain a live virus, they include:

- Shingles or chickenpox vaccines
- Measles, mumps and rubella (MMR)
- Rotavirus

- Recommendations for SHINGRIX (non-live new shingles vaccine) has not yet been made

Your family members can receive any vaccines as recommended by their doctors. You do not need to stay away from children or adults who have had recent vaccines. If you are travelling out of the country (especially tropical climate), please visit a travel clinic for further recommendations.