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Lung Transplantation ■ ■END-STAGE LUNG DISEASE AND INDICATIONS FOR LUNG TRANSPLANTATION The Lung Allocation Score (LAS) was implemented in 2005 for the purpose of prioritizing organ allocation. In this model, the United Network for Organ Sharing (UNOS) divides advanced lung disease diagnoses into four categories: (A) obstructive lung disease (including non–cystic fibrosis-related bronchiectasis and obliterative bronchi olitis), (B) pulmonary vascular disease, (C) cystic fibrosis, and (D) restrictive lung disease. Historically, obstructive lung disease was the most common indication for transplantation, but after the implemen tation of the LAS system, idiopathic pulmonary fibrosis (IPF), the most common restrictive lung disease, has become an increasingly frequent indication. In 2023, UNOS transitioned to the lung Composite Alloca tion Score (CAS) system in the United States. This system is designed to incorporate factors beyond survival, including ethical consider ations such as access and practical considerations such as efficiency, as well as efforts to optimize survival. Prior to the era of antifibrotic therapy, the average life expectancy from the time of diagnosis of IPF was 3–5 years, making patients with this disease the cohort to experience most clearly a survival benefit from lung transplantation. As a result, the LAS prioritizes patients with IPF. Similarly, patients who experience secondary effects of their lung disease, including pulmonary hypertension, right heart dysfunction, and hypercarbia, are prioritized for allocation and should be consid ered for referral for transplant evaluation irrespective of other markers of disease severity. Generally, the trajectory of decline and evolution of disease are key indicators of the appropriate timing of referral and listing for lung transplantation, rather than absolute thresholds of disease severity. However, suggested guidelines for referral have been elucidated for specific disease states. For example, in chronic obstructive pulmonary disease, the most common obstructive lung disease for which trans plantation is considered, the Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity (BODE) Index is often used as a marker of disease severity, with an index of 5 being an appropriate indication for referral for evaluation, and 7 for listing for transplanta tion. Other suggested markers for transplant consideration in obstruc tive lung disease include pulmonary function test (PFT) data, such as a forced expiratory volume in 1 s (FEV1) of <25% predicted. The frequency and severity of exacerbations of disease should also be con sidered in determining the appropriate timing of referral. With the marked advances in medical therapy for pulmonary vascular disease over the past decade, transplantation for pulmonary vascular disease has become less frequent but is still an important con sideration for patients who progress despite, or are refractory to, treat ment. Functional assessments, such as

New York Heart Association class III or IV limitations, and hemodynamic measurements, such as cardiac index <2 L/min per m2, would suggest consideration for evalu ation and listing. Patients with diagnoses generally poorly responsive to therapy such as pulmonary veno-occlusive disease should be referred early for evaluation. Patients with cystic fibrosis (CF) have historically been considered for evaluation when the FEV1 reaches ~30% predicted. However, with the exciting development of therapies targeting the CF transmembrane receptor, providers should keep in mind the potential for improvement in pulmonary function after treatment initiation. Despite this potential for pharmacotherapeutic response, referral and completion of testing should be considered so that patients are prepared for listing should they fail to see improvement or experience worsening of disease on therapy, and for patients who do not qualify for treatment. Moreover, patients who experience acceleration of acute exacerbation rate, recur rent hemoptysis, worsening functional and/or nutritional status, or

colonization with resistant bacteria should also be assessed for trans plantation irrespective of pulmonary function results.

Despite treatment progress with the development of antifibrotic therapy for IPF and other progressive fibrosing interstitial lung dis eases, these therapies do not reverse the disease but only slow the rate of lung function decline. Therefore, transplant referral for patients with IPF and other fibrosing lung diseases should still be considered at the time of diagnosis. Forced vital capacity <80% predicted or diffusing capacity for carbon monoxide <40% predicted, failure to respond to medical therapy, decline in pulmonary function tests on therapy, and functional decline are additional indications for transplant consider ation in patients with other restrictive lung diseases. Lung Transplantation CHAPTER 309 ■ ■CONTRAINDICATIONS TO LUNG TRANSPLANTATION Absolute Contraindications As experience with lung transplan tation increases, and as lung allocation policy has prioritized patients with higher acuity of disease and with diseases affecting older age groups, recipient selection criteria have become more liberal compared to prior eras. While published guidelines suggest absolute and rela tive contraindications to transplantation, these criteria are in constant evolution, and each program ultimately establishes its own selection algorithms based upon clinical expertise, experience, program size and resources, and referral patterns. Examples of absolute contraindications to lung transplantation (Table 309-1) include anatomic and technical considerations that would affect the ability to complete the transplant procedure, such as chest wall or spinal deformities or malacia of the large airways. Surgical input is critical in making such determinations. In addition, untreat able and/or irreversible organ dysfunction may preclude isolated lung transplantation. Cirrhosis of the liver, uncorrectable disease of the coronary arteries not amenable to combined surgical intervention during the transplant procedure, or other forms of uncorrectable ath erosclerotic or vascular disease may make transplantation too high risk TABLE 309-1 Contraindications to Lung Transplantation ABSOLUTE CONTRAINDICATIONS RELATIVE CONTRAINDICATIONS Surgical considerations Anatomic abnormalities not amenable to transplant procedure Age

> “ 65 years Functional status Immobility, inability to participate in physical therapy/rehabilitation Limited functional status as defined by 6-minute walk distance Medical comorbidities Untreatable, irreversible organ dysfunction

> Chronic kidney disease Active malignancy or malignancy with insufficient remission period Active bacterial bloodstream infection Infection resistant to treatment or of high risk for posttransplant morbidity/mortality (Burkholderia cenocepacia, Mycobacterium abscessus) Uncontrolled viral infection (HIV, hepatitis) Nutritional BMI <18 or >30–35 Psychosocial Untreatable, irreversible psychiatric disorder with potential to impact transplant outcome Active substance abuse Limited social supports Other circumstances that would impede ability to participate in and comply with posttransplant care History of noncompliance with medical treatment Abbreviations: BMI, body mass index; HIV, human immunodeficiency virus.

for consideration. Renal dysfunction is of particular concern given the known nephrotoxicity of calcineurin inhibitors, which are the mainstay of posttransplant immune suppression.

Relative Contraindications Age in and of itself is typically not a contraindication to transplantation at most centers. However, older patients with significant medical comorbidities may be at prohibitive risk for transplantation, and functional status and frailty may worsen in this setting. Published analyses of the Scientific Registry of Transplant Recipients, a comprehensive database of transplant outcomes, have consistently shown that functional capacity, as assessed by 6-minute walk distance, is inversely correlated with both wait list and posttrans plant mortality. As a result, most programs utilize some assessment of functional status as a criterion for transplant candidacy. PART 7 Disorders of the Respiratory System Frailty, independent of walk distance, has also been recognized increasingly as a marker of poor outcome after lung transplantation and can be assessed using a number of instruments, including the Short Physical Performance Battery (SPPB), Fried Frailty Phenotype (FFP), and others. Most studies utilizing these instruments have been con ducted at single centers. While both SPPB and FFP have been shown to correlate with the LAS, FFP has a stronger correlation, and SPPB and FFP may not correlate with each other. The Lung Transplant Frailty Scale (LT-FS) incorporates body composition and serum biomarker measure ments and has been demonstrated to be a better predictor of outcomes in the lung transplant population compared to other assessments. Patients with a history of malignancy are generally required to have experienced a period of remission prior to consideration for transplan tation. The necessary length of disease-free survival should be deter mined in the context of the type of malignancy, stage at diagnosis, and likelihood of recurrence, and often varies by program. A history of respiratory infection and colonization with resistant organisms is of particular concern in the CF and bronchiectasis populations, although it could affect patients with any advanced lung disease and a history of respiratory infection. Data on outcomes in the presence of resistant Pseudomonas aeruginosa infection are conflicting, but, in general, patients who have demonstrated a response to an anti microbial regimen, even if colonized with resistant organisms, can be considered for transplantation. Burkholderia cepacia complex, another group of gram-negative organisms that can infect patients with CF, also presents a unique concern for transplantation. Data show that B. cenocepacia (formerly known as Genomovar III) portends the highest risk after transplant, often leading to bacteremia, abscess formation, and early mortality. B. dolosa and B. gladioli may cause similar post transplant complications. Patients colonized with other Burkholderia species appear to have posttransplant outcomes comparable with the noncolonized population.

Published guidelines suggest that those programs offering transplantation to patients colonized with B. ceno cepacia do so under a research structure and after a specific discussion of the risks of transplantation in this setting with the patients. Other infectious considerations in lung transplant candidates include myco bacterial infections, particularly with rapidly growing organisms such as M. abscessus, which can lead to chronic, refractory infections and infections of the chest wall. In the case of fungal infection, assessment of the pathogenicity of the organism, resistance patterns, and, in some cases, responsiveness to pretransplant treatment is beneficial in deter mining the safety of transplantation. A history of viral infections such as hepatitis and human immuno deficiency virus (HIV) is generally not considered a contraindication to transplantation. Demonstration of adequate control of infection and responsiveness to therapy are important in preparation for transplanta tion, and development of a treatment plan that minimizes toxicity and drug interactions, in consultation with transplant pharmacy, should be completed prior to placement on the wait list. Collaborative assessment with transplant infectious disease experts is beneficial whenever the infectious history is a concern for transplant safety. Nutritional status is another important element to assess in deter mining candidacy for lung transplantation. Nutritional status has been shown to have a U-shaped relationship with transplant outcomes, with increased mortality risk associated with both underweight (body mass

index [BMI] <18) and obesity (specifically BMI >35). Consultation with nutritional experts may allow for modification of this risk prior to transplant. In some underweight patients, placement of an enteral feed ing tube and initiation of enteral feedings may be considered. Psychosocial assessment is also a key component of the evaluation of patients under consideration for lung transplantation, and a mul tidisciplinary approach with transplant social work, psychiatry, and financial care coordination is often helpful. Assessment for and optimi zation of psychiatric disorders such as anxiety and depression, which can be exacerbated in the setting of transplantation, substance abuse disorders, and compliance with medical therapy recommendations are all important parts of the pretransplant evaluation. Perioperative pain management planning in the setting of medical therapy for opioid use disorder may require additional multidisciplinary input, but the need for this management plan alone should not preclude transplantation. Transplant candidates require a strong support system given their potential posttransplant care needs. Additionally, confirmation of insurance coverage for all phases of transplant care, expected medica tion copayments, and financial resources to support other expenses in the setting of transplantation should be completed during the trans plant evaluation. Fundraising opportunities and subsidies for medica tions may need to be pursued in order to proceed safely with listing. ■ ■LUNG TRANSPLANT CANDIDATE MANAGEMENT Lung transplant candidates benefit from meticulous medical care to ensure that they are in optimal condition at the time of transplant. Oxygen is prescribed to maintain adequate systemic oxygenation to allow for moderate physical activity and exertion. Patients should be enrolled in pulmonary rehabilitation programs, if available, and should continue to participate in daily physical exercises. Patients with pulmonary vascular disease and severe pulmonary hypertension awaiting lung transplantation need special attention to maintain adequate right ventricular function. The use of pulmonary vasodilator therapy is recommended and should not be stopped prior to transplant. Patients who develop secondary pulmonary hypertension should also be assessed for the utility of direct pulmonary vasodilator therapy. Periodic assessment of right ventricular function with echo cardiography is recommended, and in patients with clearly worsening ventricular function, right heart catheterization and assessment for responsiveness to short-acting vasodilator therapy should

be considered. In restrictive lung disease patients awaiting transplant, consider ation should be given to continuation of immune modulators and/or antifibrotic therapy. Available literature does not indicate that continu ation of antifibrotic therapy in lung transplant candidates before trans plant portends an increased risk of wound dehiscence or worsened outcomes after transplant. Additionally, increased pulmonary vascular resistance can occur in these patients as the disease progresses, and acute exacerbations have been shown to be associated with severe acute decrease in right ventricular function. Steroids have been utilized in the management of acute exacerbations; however, the negative sequelae of chronic steroid use on wound healing is well established. Therefore, steroid use should be limited as much as possible and, if unavoidable, should be tapered rapidly. Patients with CF can have pancreatic dysfunction leading to diffi culty in maintaining normal blood glucose levels; uncontrolled diabe tes mellitus can make the management of posttransplant blood glucose very challenging. Therefore, optimization of diabetes management should be pursued prior to transplantation. Despite optimal medical therapy, the underlying disease in wait-listed patients will almost always continue to worsen. Prioritization of patients awaiting lung transplant is determined by the CAS system. The LAS sys tem was introduced in 2005 with the goal of minimizing wait-list mor tality and maximizing posttransplant survival. This system focused on prioritizing candidates most at risk for death while awaiting transplanta tion, and its key modeling variables focused on survival metrics. The CAS was introduced in 2023. While incorporating survival as a key com ponent, the CAS also includes variables related to special biological con siderations such as blood type and sensitization with human leukocyte antigen (HLA) antibodies, which can impact time to transplantation,

as well as variables related to ethical and practical considerations such as patient access to transplant and efficiency of the planned procedure. In addition, the CAS aims to create an allocation system that addresses prioritization more continuously, rather than placing candidates within firm boundaries or groups that create hard cutoffs for transplant access. While under the LAS patients continued to die at a rate of 10–12 patient deaths per 100 patient-years on the wait list, models of CAS allocation suggest expected improvements in both wait-list mortality and post transplant survival, as well as improvements in equity in access to trans plantation. Further studies of the actual results after implementation will be needed to confirm these expectations. A major consequence of improved efficiency in matching the sickest patients to the available pool of donors has been an increased use of extracorporeal membrane oxygenation (ECMO) devices to bridge the most critically ill patients to transplant. Mechanical circulatory sup port with ECMO allows for patients to be potentially weaned from the ventilator, to maintain physical activity and ambulation, and to be in a state of greater robustness as they await transplant. The posttransplant survival rate of patients bridged to transplant with ECMO is equivalent to those transplanted without the need for ECMO in experienced, high-volume centers and better than patients who had previously been transplanted directly from mechanical ventilatory support. Further more, with improvements in membrane oxygenator technology, plat form miniaturization, and improvements in cannula design, outcomes continue to improve. ■ ■DONOR CONSIDERATIONS The ideal lung donor has remained constant since the inception of lung transplantation in the 1980s (Table 309-2). A donor between 25 and 40 years of age, with a Pao2/Fio2 ratio >350, no smoking history, a clear chest x-ray, clean bronchoscopy, and minimal ischemic time is considered the ideal donor; however, it is quite rare that a donor meets all of these criteria for transplantation. In fact, the vast majority of donor lungs used for transplant fall outside these ideal lung donor criteria as established more than three decades ago. Donors must have irreversible brain injury, and the majority of donors are brain dead.

Only 20% of all donors with brain death are suitable lung donors due to the development of severe neurogenic pulmonary edema and increased susceptibility of potential lung allografts to infection and injury. Absolute contraindications to lung donation include radiographic evidence of chronic lung disease such as emphysema and pulmonary fibrosis. Other absolute contraindications include active malignancy, a donor history of severe asthma requiring multiple hospitalizations, and positive HIV status. Relative contraindications include older donor age, severe thoracic trauma with extensive pulmonary contusions, the pres ence of pulmonary hypertension, and prolonged donor hypotension or acute hypoxemia. The standard lung donor evaluation includes a donor medical and social history, physical examination, and laboratory examination. Chest imaging is mandatory, as are arterial blood gases, bronchoscopy, and serologic tests for cytomegalovirus (CMV), Epstein-Barr virus (EBV), hepatitis B and C, HIV, Toxoplasma, rapid plasma reagin, and herpes simplex virus. The presence of consolidation and atelectasis, while not absolute contraindications to transplant, are often difficult TABLE 309-2 Characteristics of the Ideal Lung Donor Donor age <55 years ABO compatibility Identical Chest radiograph Clear Pao2:Fio2

> 300 on PEEP 5 cmH2O Tobacco history <20 pack-years Chest trauma Absent Evidence of aspiration Absent Prior thoracic surgery None Sputum Gram stain Negative Bronchoscopy findings No purulent secretions Abbreviation: PEEP, positive end-expiratory pressure.

to assess with noncontrast radiographic imaging alone. Ventilation parameters must be evaluated to ensure adequate compliance of the donor lungs, with peak airway pressures <30 cmH2O being ideal. Direct on-site inspection of the lungs and assessment for nodules, compliance, and full expansion are the final necessary steps before acceptance of donor lungs for transplant.

More recently, there has been an expanded use of allografts from donors after cardiac death (DCD) due to the ability to rehabilitate donor lungs using ex vivo lung perfusion (EVLP). DCD donors are patients who present with irreversible brain injury but without overt brain death. The potential donor allografts are often exposed to a period of prolonged warm ischemia during the donation process; there has been a concern about early graft dysfunction after DCD donation. Steen and colleagues in Lund demonstrated that EVLP could be used to assess these marginal donors prior to transplant. The landmark publication of the Normothermic Ex Vivo Lung Perfusion in Clinical Lung Transplantation trial in 2011 generated renewed interest in DCD lung donors. The group from the University of Toronto was also able to demonstrate that brain-dead donors with unacceptable donor lung parameters could be rehabilitated with the use of EVLP. They were able to salvage up to 50% of selected unsuitable donor lung allografts with the use of acellular normothermic hyperosmotic perfusion with excel lent short-term outcomes. Lung Transplantation CHAPTER 309 Donor Management Brain death causes severe perturbations in the potential donor lung allograft function. The development of severe pulmonary edema often accompanies brain death. The hemodynamic instability and neurogenic shock that can accompany brain death are also major stressors on the preservation of donor allograft function. The primary goal of donor management is, therefore, the maintenance of hemodynamic stability and preservation of donor lung function. Judi cious fluid resuscitation and avoidance of excessive resuscitation should be employed. Volume replenishment should be limited to maintain the central venous pressure between 5 and 8 mmHg.

In general, crystalloid fluid boluses are to be avoided. Diabetes insipidus is common in donors and requires the use of intravenous vasopressin to prevent excessive urine loss. In general, blood transfusions should be avoided; however, if necessary, CMV-negative and leukocyte-filtered blood should be used whenever possible. Hypothermia should be avoided as it predisposes to ventricular arrhythmias and metabolic acidosis. Excessive oxygen delivery should be minimized to prevent freeradical injury to the potential lung allograft. Positive end-expiratory pressures on the ventilator should be maintained to avoid the develop ment of atelectasis. More recently, airway pressure release modes of ventilation have been utilized to preserve lung function and minimize barotrauma from prolonged ventilation. ■ ■PROCUREMENT OPERATION Prior to incision, a thorough bronchoscopic evaluation is completed. The anatomy of the donor airways is defined. Any secretions that may be present are evacuated, and the airways are examined to rule out the presence of any lesions or masses. The epithelial lining is inspected for evidence of excessive friability and hemorrhage, which may indicate significant infection. A median sternotomy incision is employed to access the chest for lung procurement. The pleural spaces are opened and both lungs are inspected, palpated, and gently recruited to evaluate for suspicious nodules, consolidation, and/or pulmonary infarction. The donor is systemically heparinized, and the main pulmonary artery is cannulated. Fifteen minutes prior to initiation of the explant, prostacyclin is introduced into the main pulmonary artery and allowed to circulate through the lungs. This vasoreactive prostanoid helps to ensure adequate pulmonary flush by dilating the pulmonary vascu lature. The heart is arrested first, then the pulmonoplegia solution is instilled into the lungs at a low controlled pressure. Topical iced-saline solution is instilled into both pleural spaces. After the heart has been explanted, the individual pulmonic veins are flushed retrogradely. The lungs are then re-expanded, the trachea is clamped, and the explanted allograft is stored in ice-cold saline solution for transport. If the right and left lungs are being procured for different recipients, the posterior

 left atrium, the main pulmonary artery, and the left main-stem bron chus are divided to separate the right and left lungs, and the organs are stored and shipped separately. New preservation technologies and studies of optimal temperature for storage and transport may allow for longer transport times and time to implantation. Investigations of the impacts of these advances are ongoing. ■ ■RECIPIENT OPERATION AND EARLY POSTTRANSPLANT CONSIDERATIONS Recipient Operation The recipient operation can be divided into two parts. The first part involves the explant of the native lung, and the second part involves the implant of the new lung. There are generally three main surgical approaches to the completion of the operation: a right or left thoracotomy, a transverse thoracosternotomy (clamshell), or a median sternotomy. These approaches are all favored by various centers for different benefits. The thoracotomy approach allows for explant and implant of donor lungs without the use of cardiopulmo nary bypass (CPB) and is often the preferred approach for single-lung transplant. The clamshell incision offers the advantages of increased exposure compared to either thoracotomy or median sternotomy but comes at the cost of greater morbidity and postoperative wound complications. This incision can be used to perform bilateral lung transplants and allows for the possibility of avoiding CPB. A median sternotomy approach can be used to perform bilateral lung transplant. This approach offers the advantage of fewer wound complications, less postoperative pain, and flexibility with more complex or concomitant cardiac procedures at the time of lung transplant. This approach man dates the use of CPB. The routine use of CPB allows for early pneumo nectomies without hemodynamic compromise and can significantly reduce the ischemic time to the second allograft. Additionally, overcir culation to the first allograft can be minimized with the routine use of CPB. Others prefer to avoid CPB as avoidance may be associated with

decreased need for blood product administration and lower incidence of primary graft dysfunction. Over the past 5 years, there has been a movement away from CPB for mechanical circulatory support toward ECMO. ECMO is an alter native strategy for providing hemodynamic and pulmonary support of the patient undergoing lung transplantation. The key difference between CPB and ECMO is the ability to salvage shed blood with CPB, the use of a blood reservoir with CPB, and the ability to filter air from the venous system before it is delivered to the arterial circuit with CPB. This flexibility is provided by exposing the blood in the system to a much larger foreign surface and has been associated with significantly increased inflammation and tendency for thrombosis. Therefore, ECMO requires much lower levels of anticoagulation than CPB. The advantages of ECMO-supported lung transplantation are a tendency toward less blood product administration and, in situations in which CPB support periods are longer (>180 min), a tendency to decreased rates of primary graft dysfunction. Data suggest that the use of ECMO for mechanical support during lung transplant is safer than lung transplant with no mechanical support, and the recommendation is to use ECMO for all cases. Its use may especially be helpful for cases that are expected to require longer support times. Careful attention to avoid the entrainment of air into the circuit is mandatory throughout the ECMO support period. Anesthetic monitoring for lung transplant should include arterial pressure monitoring, pulse oximetry, continuous electrocardiographic monitoring, temperature monitoring, and urine output monitoring. Large-bore IV access and central venous access are vital to manage the patient safely. On a selective basis, pulmonary artery pressure monitor ing and transesophageal echocardiographic monitoring may be useful. For patients without the planned use of CPB, double-lumen endotra cheal tubes are mandatory, whereas they can be avoided for patients transplanted on CPB. Once access to the thorax has been completed, the hilar structures are isolated and divided. The bronchial anastomosis is completed first, and the anastomosis is checked to ensure that it is secure by insufflat ing the lung gently while keeping the anastomosis under saline solution to observe for bubbles. The donor left atrial cuff incorporating the pulmonary vein is connected to the native left atrium, and the donor right or left pulmonary artery is connected to the native pulmonary artery. After completion of the vascular anastomoses, the lungs are gen tly reperfused. During this early reperfusion period, lung-protective ventilation strategies are employed and oxygen tension is reduced. The patient is transitioned to normal ventilation, drains are placed in the thoracic cavity, and the wounds are closed. Induction of Immunosuppression Initiation of immunosup pression starts with induction of the patient under general anesthesia. Many programs utilize an induction agent (most commonly an inter leukin 2 [IL-2] receptor/CD25 antagonist, but antithymocyte globulin, anti-CD52 monoclonal antibodies, or other induction agents may also be used), and systemic corticosteroids and purine modulators are administered after induction is complete. If an IL-2 receptor antagonist is utilized for induction, a second dose is administered 4 days after the original dose. An additional dose of methylprednisolone is adminis tered after allograft reperfusion in the operating room. Three-drug immune suppression is initiated with a calcineurin inhibitor, purine modulator, and continued systemic corticosteroids. In patients with severe acute renal dysfunction, calcineurin inhibitor initiation may be delayed. Perioperative Considerations and Complications Early mor bidity and mortality after lung transplant most commonly are sequelae of primary graft dysfunction or infection. Very rarely, hyperacute rejection has been observed; however, with the implementation of robust systems to ensure ABO and HLA compatibility at the time of transplant, the occurrence of hyperacute rejection is extremely uncom mon. Primary graft dysfunction (PGD) encompasses a constellation of findings that result in poor early graft function after transplant. This phenomenon is often the consequence of ischemia-reperfusion injury in the allograft and is not related to infection or rejection. It is char acterized by a diffuse pattern of infiltrates on the chest x-ray and poor

pulmonary gas exchange with Pao2:Fio2 ratios <300, with severe PGD characterized by diffuse severe infiltrates and a Pao2:Fio2 ratio of <100 at 72 h posttransplant. Most cases of PGD are mild and self-limiting, resolving with supportive care. However, if the PGD is severe and wors ening despite maximal medical therapy, diuresis, inotropic therapy, maximal ventilation support, and paralysis of the patient, mechanical circulatory support with ECMO can become necessary. The incidence of severe PGD has been steady over the past two decades at approxi mately 10–15% in most programs. Severe PGD at 72 h posttransplant portends an increased mortality risk and is a risk factor for chronic lung allograft dysfunction (CLAD). Bacterial, viral, and fungal infections are leading causes of morbid ity and mortality in lung transplantation. The lung is one of the few solid organs that is in continuous contact with the environment. Each breath has the potential to introduce new organisms, and the reduced lymphatic function and mucociliary clearance in the transplanted lung increase the risk of serious infection. The highest incidence of infection is early after lung transplant and coincides with the inten sity of immune suppression. Early infections, occurring within the first month after transplantation, are commonly bacterial (especially gram-negative bacilli) and manifest as pneumonia, mediastinitis, urinary tract infections, catheter sepsis, and skin infections. Patients can develop pathogenic infections with organisms associated with pretransplant colonization, and perioperative antibiotic regimens are often deployed to address this. Viral infections, and CMV infections in particular, can lead to severe recipient disease and early loss of graft and life. The majority of transplant programs employ antiviral prophylaxis in the early transplant period to avoid such complications. Invasive fungal infections peak in frequency between 10 days and 2 months after transplantation. Fungal prophylaxis regimens in the early posttransplant period vary widely. Treatment consists of inhaled amphotericin B in the setting of airway infection and/or azole therapy with more advanced or invasive disease. The institution of prophylaxis with oral trimethoprim-sulfamethoxazole (or atovaquone or inhala tional pentamidine for sulfa-allergic patients) has effectively prevented Pneumocystis pneumonia. The risk of Pneumocystis infection is highest

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