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A Personal View on the History of Lung Transplantation

Professor Paul A Corris
Newcastle University

Lung transplantation experienced a roller coaster of a ride during its clinical development, having experienced a difficult childhood and traumatic teens, and finally emerging as a gloriously successful treatment for advanced lung disease in adulthood. I am minded to compare it with the development of a Medoc premier cru classé in this respect!

The first successful attempt at isolated human lung transplantation was performed in the USA by James Hardy in 1963. I choose to use the word success with the same confidence as Humpty Dumpty in Lewis Carroll’s Alice through the looking glass who said “when I choose a word it means exactly what I choose it to mean.” I say this because some twenty more years later the Toronto group led by Joel Cooper claimed the first successful clinical examples of isolated lung transplantation and certainly their patients survived longer and left the hospital.... Nevertheless Hardy is usually credited with the important first clinical step, in an era when there was no concept of brain stem death so, unbeknownst to him, he was also the first to use a DCD donor of which more later. What we do know after Hardy’s “success” was that over the next 15 years the literature recorded 40 further attempts all of which failed, largely as a result of primary graft failure, bronchial anastomotic breakdown and multiorgan failure – problems which seemed insuperable. By the late 1970s interest in lung transplantation as a clinical prospect had waned, contrasting with major developments in renal, liver and cardiac transplantation.

The introduction of cyclosporine as a highly effective immunosuppressant heralded renewed interest in lung transplantation, notably at Stanford University. The combination of effective safe immunosuppression, the development of heart lung transplantation ensuring a viable blood supply with a tracheal anastomosis by coronary bronchial anastomoses and a meticulous and rigorous approach in the laboratory under Shumway’s direction led to clinical success.

In 1982 the Stanford group reported success in a small series of patients with advanced idiopathic pulmonary hypertension.

From these modest beginnings, lung transplantation has developed into a well-established treatment option for a wide range of respiratory conditions including COPD, lung fibrosis and, perhaps most notably, cystic fibrosis. Moreover, advances in surgical technique have permitted the re-introduction of isolated lung transplantation initially as single, then bilateral followed by lobar transplantation. Isolated lung transplantation, in particular bilateral transplantation, is now by far the most common surgical approach in the current era.
Success in long term, survival with a good life quality following single lung transplantations was first reported in 1986 by Joel Cooper and colleagues from Toronto and in 1987 the Newcastle team performed the first successful isolated lung transplantation in Europe on a 50-year-old lady suffering from advanced Langerhan’s Cell Histiocytosis who was a patient of mine both before and following transplantation.

As the early lung transplantation recipients aged, it was recognised that many began to develop progressive irreversible airflow obstruction which on lung biopsy was shown to be due to obliterative bronchiolitis. Initially thought to be a manifestation of chronic allograft rejection alone, it is now recognised to represent allograft dysfunction as a consequence of diverse insults including infections and gastro oesophageal reflux. It remains the most important barrier to improving long-term outcomes of lung transplantation and is a major focus of international research.

Recently, use of the macrolide antibiotic azithromycin, which also has anti-inflammatory properties, has been shown to be able to halt the progress of this condition and improve lung function in approximately 50% of patients.

It is a comforting fact that over the last 25 years we have witnessed huge improvements in survival following lung transplantation. In the late 1980’s a recipient only had a 50% chance of living one year whereas now 40-50% of recipients can expect to live over 10 years. Moreover, the quality of life gained is excellent with near normal restoration of exercise tolerance and the ability to fully participate in work and active recreations.

Many female recipients worldwide have now had successful pregnancies after lung transplantation.

The shortage of donor lungs remains a problem and despite increases in the number of potential donors joining national donor registries, the number of lungs from brainstem dead donors has not increased significantly in many countries. New approaches, including the use of lungs from non-heart beating donors (the DCD donor pool I spoke of when recalling Hardy’s exploits) have increased the donor pool. More recently, the size of the donor pool has further been boosted by the technique of reconditioning lungs that are not safe to use for primary lung transplantation during ex vivo perfusion and ventilation. It would be remiss of me not to note the work of Stig Steen from Lund and Shaf Keshavjee from Toronto in developing this approach.

The last 25 years have seen lung transplantation grow from a procedure associated with little success to an established therapeutic option for patients with advanced lung disease. It has brought hope on the basis of its success to many patients. It is truly a remarkable story of medical advancement in the field of respiratory medicine and I am proud to have played a small role.
Dedication and Thanksgiving

Vincent G Valentine, MD
University of Texas Medical Branch

About a century prior to the first human lung transplantation by Dr Hardy and his collaborators, a dedication of the National Cemetery at Gettysburg occurred on November 19, 1863. Selected for the keynote speaker was the former president of Harvard, leader of the Greek revival and one of the most noted and eloquent orators of that time, the Honorable Edward Everett. In response to the decision to invite the President, Abraham Lincoln, for a few appropriate remarks, someone retorted, “I don’t know—all he does is tells jokes. I think he will be an embarrassment.” Everett’s address lasted for two hours. Lincoln’s brief remarks took a little more than two minutes. Today, when we refer to the Gettysburg Address, we think of Lincoln’s speech.

Although November is a month celebrated with two other perhaps more recognizable holidays—Veteran’s Day or Day of Peace as it is known elsewhere, and of course, Thanksgiving—Lincoln’s Gettysburg Address is what I suggest you revisit. Even today, we can pay homage to its meaning and how it and these holidays of gratitude link us to what we’ve dedicated our lives.

Lincoln’s eloquent speech, albeit seemingly abstract, was as deliberate and precise as a swinging pendulum taking us not only to and fro in time but also back and forth in life and death. It begins with his timeless two rhyming words sweeping us to our past.

“Four Score and seven years ago,” tolls like a cathedral bell beckoning our attention. It is a reference to the American Revolution and the Declaration of Independence (1863 – 1776= four score and seven years). Immediately we are reminded of our inter-relatedness by the familial and obstetrical imagery that follows. Reference to “our fathers” is a family relationship emphasizing that we are descendants of these founders. With obstetrical analogies, “brought forth on this continent a new nation conceived in liberty” we take pride in the life of this land. From here Lincoln culls out of all possibilities the first of the self-evident truths...“all men are created equal.” And with that we know what the war is ultimately about—giving those who have died the greatest possible honor by advancing Thomas Jefferson’s principle that these fallen have enabled this nation yet another new birth.

After only a single sentence, Lincoln’s words swing us out of our past and into the present. “Now we are engaged in a great civil war...” Time is suspended and dangles without ties to the battle, the cemetery, the confederacy or the army of the Potomac. Instead we are grounded in the immediate occasion, “we are met to dedicate a portion of that battle-field” and we are resolved to acknowledge the seamless connectivity of life and death, “...for those who here gave their lives that that nation might live.”

With a somber cadence Lincoln acknowledges, “It is altogether fitting and proper” to meet for this dedication, yet he subverts that expectation with grave repetitive sacred phrases. “But, in a larger sense, we cannot dedicate, we cannot consecrate, we cannot hallow this ground.” We can’t meet for this dedication, because it has been done already by the brave acts of those who fought here. His rhetorical strategy was an antithesis contrasting the living with the dead, and humility with pride, “The world will little note, nor long remember what we say here, but it can never forget what they did here.” The latter four words are his summary of the battle and clearly he views that their actions speak louder than any words expressed that day.

From the present, “We have come to dedicate a portion of that field, as a final resting place...” the pendulum
takes its final swing toward the future in a rededication, “to the great task remaining before us…” The standard eulogy developed in Ancient Greece by Pericles gives a transformative theme of praise for the dead and advice for the living. Lincoln reverently honors the valiant dead and advises that we follow in their devotion such that his focus shifts from the nation to the world. Lincoln never specifies the “great task’ remaining. This is a subject for interpretation.

What about our work? What about honoring the dead, the dying patients and the organ donors that might motivate in us the devotion Lincoln encourages? What of the great task he suggests? Perhaps one could be to improve our ability to care for others. Another greater task may just have a personal meaning for health care providers, patients, leaders or anyone in the world.

Perhaps we should focus on what we do rather than what happens. This process is more valuable and may prove more successful than simply reporting data. In other words, instead of stating our outcomes and simply recording the results, we should explain our data and improve the process for what’s best for all.

The Honorable Edward Everett was the first to recognize this in a letter to Lincoln, he writes, “I should be glad if I could flatter myself that I came as near to the central idea of the occasion in two hours as you did in two minutes.” The ever so humble Lincoln replied, “In our respective parts yesterday, you could not have been excused to make a short address, nor I a long one. I am pleased to know that, in your judgment, the little I did say was not entirely a failure.”

Every year around Thanksgiving I read from the coveted Pulitzer Prize winning book, Abraham Lincoln by Carl Sandburg. Chapter 38, Lincoln Speaks at Gettysburg, is one I encourage all to read, paying particular attention to the final six paragraphs. In these final words there is a “...tall old clock in a quiet corner telling time in a tick-tock deliberation.” Whether, “…the orchard branches hung with pink-spray blossoms or icicles of sleet, whether the outside news was seed time or harvest, rain or drought...,” births or deaths, air moving in and out of airways effortlessly like the swing of a pendulum. “In a row of graves there is an unidentified boy who had listened to its tick-toc and learned to read its minute and hour hands. His years measured off by the swinging pendulum had gone awry and swallowed with other men into a deep sea of man-made smoke and steel.

“The mystery deepened and moved with ancient music because a solemn Man of Authority stood at the tombs of the unknown soldiers and spoke the words. We cannot consecrate, we cannot hallow this ground.” The brave men, living and dead, who struggled here, have consecrated it far above our poor power to add or detract... from these honored dead we take increased devotion to that cause for which they gave the last full measure of devotion.

Shortly after Lincoln’s return from Gettysburg, he was sick with small pox. He quipped, “I now have something I can give everybody.” Contagion.

Happy Thanksgiving, and a special Thanksgiving to my writer friend, Julia Hayes

http://avalon.law.yale.edu/19th_century/gettyb.asp
Contagion: Bugs, Drugs and Hugs

Lara Danziger-Isakov, MD, MPH
Cleveland Clinic

In September, Stanley Martin extolled the virtues of influenza vaccination for patients and practitioners. Now that everyone has “rolled up their sleeves” to protect their patients and themselves from influenza, respiratory season kicks into gear in the northern hemisphere (my apologies for the skewed view to our colleagues down south).

Respiratory viruses have gained increased attention in the past several years with multiple studies showing both immediate impact and long-term complications including their association with the bronchiolitis obliterans syndrome. Novel therapies for specific viruses are currently under investigation at many centers with ISHLT members. These include but are not limited to ALN-RSV01 for respiratory syncytial virus, CMX-001 for adenovirus, poly-ICLC for influenza and other respiratory viruses, and various combinations and formulations of antivirals for influenza treatment. While we wait for the research on novel antiviral therapies to combat these viruses, here are some simple measures to implement as a team with our patients to prevent respiratory viruses and promote a happy and infection-free holiday season.

For your patients:
1. Vaccinate yourself, your team, your patients and their families against influenza
2. Instruct your patients and their families about hand hygiene
3. Discuss risk behaviors for respiratory viruses
   - Remind families that they are a circle of protection around the transplant recipient
   - If someone in the family is sick, avoid direct contact until they recover
   - For children, communication with schools or day-care is essential
4. Remind your patients to report symptoms as early as possible to the transplant team

For your teams:
1. Hand hygiene before and after every patient contact
2. Keep abreast of the local, regional and national trends of current circulating pathogens
3. Consider isolating patients with respiratory symptoms in your clinics and hospitals and tailoring isolation to the pathogens recovered
4. Stay home or avoid patient contact if you are ill
The Pulmonary Transplant Council is busy with an exciting variety of ongoing and new projects under the leadership of Lianne Singer (Chair), David Weill (Vice Chair) and Michael Mulligan (Secretary).

We have two novel Registry-based projects under development. Our Registries and Database Workgroup led by Shaf Keshavjee is actively working on a DCD registry with UNOS which will link to the ISHLT registry. The Quality of Life Workgroup, led by Roger Yusen and Lianne Singer, is working on the QUILT (Quality of Life in Lung Transplantation) registry pilot study, which will link patient health-related quality of life measurements with ISHLT registry data.

The Antibody-Mediated Rejection Workforce led by Debbie Levine and Adriana Zeevi is working to define, set a research agenda and explore management of this emerging entity, similar to what has been achieved by our cardiac colleagues. Another group, led by Shaf Keshavjee and Michael Mulligan, is developing guidelines for state-of-the-art management of the deceased lung donor.

We actively collaborate with other societies. With the ACCP, we administered a survey of palliative care barriers and practices in lung transplant candidates, which was presented at ISHLT 2011 and is being prepared for publication. With the ATS and the ERS, we have developed an updated review of chronic allograft dysfunction, with key concepts to be presented at a pre-meeting symposium at ISHLT 2012 in Prague.

The ISHLT Academy: Core Competencies in Lung Transplantation at ISHLT 2011 in San Diego was a resounding success thanks to the hard work of our Education Workforce led by Chris Wigfield, and our outstanding international faculty. We anticipate an excellent meeting in 2012 with an abundance of high-quality abstracts in lung transplantation and advanced lung disease.

In the meantime, we have been able to keep up a lively discussion through our Google group, ably administered by Remzi Bag, which is a great forum for the difficult questions all of us face as lung transplant clinicians. We invite all interested members to join the conversation, whether online or face-to-face in beautiful Prague!

"It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair, we had everything before us, we had nothing before us, we were all going direct to Heaven, we were all going direct the other way—in short, the period was so far like the present period, that some of its noisiest authorities insisted on its being received, for good or for evil, in the superlative degree of comparison only.

There was a king with a large jaw and a queen with a plain face, on the throne of England; there was a king with a large jaw and a queen with a fair face, on the throne of France. In both countries it was clearer than crystal to the lords of the State preserves of loaves and fishes, that things in general were settled for ever.

— Charles Dickens"
From the Worst of Times to the Best of Times and Back with IPF

David Weill, MD
Stanford University Medical Center

Idiopathic pulmonary fibrosis (IPF) is a disease that has a poor prognosis with a 3-year median survival of nearly 50%. Unfortunately medical therapy for this disease has been disappointing, resulting in no change in outcomes for a quarter century. The only two interventions that have improved survival in IPF are lung transplantation and enrollment in therapeutic clinical trials (Nathan et al, Chest 2011;140:221-229). Wait list mortality has decreased since the advent of the lung allocation scoring (LAS) system and likely has the greatest impact on those with IPF given that group’s high wait list mortality. An important concern remains however whether the improvement in wait list mortality has resulted in sicker IPF patients being transplanted, a group known to have worse postoperative outcomes. This consideration must be balanced against the limited therapeutic options for patients with IPF—sicker patients not receiving a lung transplant will progressively suffocate and ultimately die.

The destiny of IPF patients pursuing lung transplantation changed in May of 2005 when UNOS implemented the LAS. Developed to address the dual goals of reducing wait list mortality and allocating lungs to those with the greatest chance of post-transplant survival (the “transplant benefit”), the LAS most dramatically benefits those with IPF, a group that has traditionally had the highest waiting list mortality and in whom transplantation most obviously changes its survival trajectory. Therefore in some ways, the period since implementing the LAS represents the best of times for patients with IPF. Less likely to die on the waiting list and able to receive lungs during periods of precipitous declines requiring hospitalization, mechanical ventilation, and even forms of extracorporeal membrane oxygenation, IPF patients now occupy most of the high LAS territory on program’s waiting lists. As a result, IPF is the most common indication for lung transplantation. According to the most recent UNOS data, IPF patients represent 40% of all transplants performed in the United States. This will likely increase, given the increased prevalence of interstitial lung disease and comfort with lung transplantation as a viable therapeutic option. In fact, conversations with my colleagues reinforce this point; many say lung transplantation has become “all about IPF”. This may be hyperbole but there is some truth to it. Lung transplantation may not be “all about IPF” but it’s certainly more about IPF. Which begs the question: is this a good thing? Change you can believe in, especially from the worst of times prior to LAS for these patients?

Since the LAS gave IPF a more prominent place in all of our practices, any analysis of IPF and lung transplantation begins with an analysis of the LAS. What do we know today about how well the LAS is working? The answer to this question depends on how one defines “working”. It is clear that time on the waiting list has been shortened (Merlo et al, JHLT 2009;28:769-75) and that consequently waiting list mortality has decreased...
However, our group looked at the effect of the LAS on one-year survival and found that scores >60 were associated with worse outcomes (Liu et al, AJT 2010; 10:915-920). The Merlo analysis reached similar conclusions demonstrating only a 75% one-year survival in those with an LAS>46. With regard to both of these studies, there is one important caveat: neither attempted to factor in the potential lives saved due to reduced waiting list mortality rates in combination with what appears to be a worsened one-year survival in higher LAS groups. One can say, however, that it is quite possible that the LAS system may prioritize sicker patients (often those with ILD) who have outcomes known to be poorer, which in effect would increase the emphasis on preventing wait list mortality at the expense of reduced survival following transplantation. A less important but relevant consequence of a system preferentially transplanting sicker patients is higher resource utilization, manifested by higher hospital charges and lengths of stay in the higher LAS groups (Arnaoutakis et al., JHLT 2011;30:14-21).

Given what has been presented here, what’s the bottom line? The implementation of the LAS has represented one of the most promising developments in lung transplantation, especially for ILD patients who are rapidly deteriorating. In the past, these patients had little hope and many of us simply watched them suffocate to death with very few options during the worst of times. Now, however, using whatever means (e.g. mechanical ventilation and/or newer types of ECMO) at our disposal to keep these patients alive while awaiting transplant is a winning strategy. One day soon we will have our “Tale of Two Outcomes” in the lung transplant field. We will also have “our LVAD” as the study of artificial lungs advances, and one can easily envision further evolution towards a “bridging strategy” than the one currently in our armamentarium. However, with this excitement comes responsibility in the form of paying particular attention to proper organ utilization. The best still comes with the worst, as a community, we should carefully study the LAS system, make refinements where necessary, and determine when offering transplantation to a very sick recipient is not prudent. These are tough decisions to make, but we can all agree that just because we can do something doesn’t mean we should. If we want lung transplantation to be more closely associated with the outcomes seen in other solid organ transplants, measures to improve our understanding of the LAS and how it should best be used is a step in the right direction.
A Blessed Attitude

Ami Shuford

As children, we are taught that death is something a long way off on the horizon. It is something you know exists, and are never supposed to be confronted with until you are “older”. It isn’t until you are hit head-on with the possibility of death that you realize the relativity of growth and how an individual’s spirit creates a lasting impression on all of the lives that he has touched.

My father’s destiny could have been written by the doctor’s diagnosis of Idiopathic Pulmonary Fibrosis, but Allan Shuford chose to pen his own path from those darkest days in 1996 to nearly twelve years post-transplant. No matter how bad my Dad felt or how hard it was for him to breathe, he always kept a positive attitude. His attitude was that he knew that he could be worn down and tired of being sick, but his illness would never “beat” him. He read constantly, chronicling his daily routine, feelings and expectations in a journal. He made sure he stayed involved in all of the things that parents traditionally are. He couldn’t coach baseball, but he made sure he was at the local baseball field each summer evening to keep score for my brother’s games. He was in a wheelchair and tied to an oxygen tank at that point, but it never dampened his spirit or involvement with the family.

For me at age 9, it was my expectation that once transplanted he would be miraculously transformed into the vibrant active man he once was. I wish that I could say that was exactly how it happened, but of course that only happens in fairy tales.

After transplant he worked hard to gain back the strength he’d lost, a long shot at best, but he kept at it and eventually was able to resume his volunteer work at our high school. He also worked with Louisiana Organ Procurement Agency on a regular basis urging people to become organ donors and using his story as an inspiration to let other people know there was hope when things seemed most bleak. Our family began to travel again, spending quality time together visiting the places we all loved—Disney World with Lego Man, Nags Head, and New York City. Dad was a huge Yankee fan, so if
the opportunity arose to go to a game in Yankee Stadium, you can bet he’d do anything in his power to be there.

I have no doubt that life would have been totally different had there not been a lung transplant. Obviously his life would have been cut even shorter than it already was. My mom, brothers and I would have struggled with the overwhelming loss and the lack of direction and inspiration that my father gave us. I wouldn’t have had him at my high school graduation, he wouldn’t have been at my mother’s side when my brother Andrew married his high school sweetheart, and he wouldn’t have been in the hospital waiting room when his first grandchild, Emma Rose, came into the world. These seem like normal adventures through life but my dad was able to experience all of these things against long odds and they were each monumental.

I often encounter people who ask about the transplant process, or who have had similar experiences to my own, or think it is the most alien thing in the world. I always tell them the same thing—not having a transplant was not an option to my dad or the family, because my father had a life to live and this was simply something we had to overcome. Benjamin Hochman, a writer for the Denver Post and friend of our family, recalled a conversation he had with my dad that sums up his feelings and ours: “A lot of people say, ‘You’ve been through (heck).’ And I’ll say, ‘You don’t understand — I’m blessed.’” (Hochman, 2009 Denver Post).

Today, I am 24-years-old, currently studying Respiratory Therapy at Delgado Community College in New Orleans, with plans to graduate next December. My dad’s experiences have led me to pursue this path, and it gives me great satisfaction to know that I will be able to help patients the way my dad’s health care team cared for him.
The Tables Are Turned

Nancy J Addis
Pearland, Texas

How did this happen?
From being caregiver and nurturer to
Being the recipient of care and nurturing?

It happened. Who knows why?
No longer able to give hands on care
Now expressing concern by sharing words of comfort.

When did this happen?
Independent, healthy, strong-willed
(or was that stubborn) woman
Becoming unhealthy, unsteady and short of breath?

It happened. Who knows when?
Now, oxygen and walker are used to help
Return independence and bright outlook on life.

What happened to that goal-oriented person?
The one with the authoritative strong voice,
lecturing students
Now with a weak quavering voice?

It happened. What need is there for
Authoritative voice when there are no students to
Teach or employees to manage?

Where did that nurse go?
You know the one, the first to be called by family
To render care or give advice concerning health concerns.

It happened. The nurse did not go away.
Advice is still free with no strings attached
Only love and concern for those she may console.

Is she still here? Look under
The white hair, into the weatherworn face
Do her eyes tell you she is still there?

She may no longer be the caregiver
Knowing that she is the recipient of those special
Gifts when care and concern now come her way

Still the strong-willed, decisive,
Organized person she has always been
Nancy is still here.
Lung Transplantation for Cystic Fibrosis – Evolution

Cecilia Chaparro, MD
Toronto General Hospital

The first successful lung transplant was performed in 1983 in a patient with pulmonary fibrosis [Toronto Lung Transplant Group N Engl J Med 1986; 314:1140]. This opened the door to lung transplantation as a therapy for patients with end stage lung diseases.

Patients with cystic fibrosis (CF) were not considered optimal candidates for transplant due to fears regarding lung infection and the “systemic” nature of their disease, that is extrapulmonary involvement specifically diabetes and malabsorption with poor nutritional status. Two years after the initial successful lung transplant, the first lung transplants in CF patients were performed [Scott J. Lancet 1988;2:192,]. The expected complications were evident. They included those related to the surgical procedure itself: more bleeding and difficult dissection as well as early post-transplant complications with airway dehiscence due to infection [Bremmer R. Am Surg 2001;67:1136]. Gram negative bacilli [Brooks R. Am J Med 1985;79:412] were the most frequent cause of infection amongst which *Burkholderia cepacia* was associated with increased mortality [Snell G. Chest 1993;103:466; Chaparro C. Am J Respir Crit Care Med 2001;163:43].

Other early post-operative complications included gastrointestinal abnormalities such as delayed gastric emptying, distal intestinal obstruction syndrome (DIOS) and malabsorption that made it difficult to achieve and maintain therapeutic levels of immunosuppressants and other medications [Scott J. Lancet 1988; 2: 192-194].

Despite all of these concerns, transplantation for CF patients flourished and today over 5,500 lung transplants have been performed in CF patients [Christie JD. J Heart Lung Transplant. 2011;30:1104]. The most recent ISHLT report showed that the conditional half-life survival of patients surviving at least 1 year was significantly better in patients with CF (10.4 years). Causes of death post-transplant in patients with CF are not different from those of other lung transplant recipients. Infection is the most common early post-transplant and chronic rejection the most common in long-term survivors.

Transplant programs around the world have gained expertise in the management of these patients before transplant in preparation for their surgery and after transplant in managing them with all of their associated complications. Some of the challenges today include:

1. **Infections.** Formerly, the most common organisms causing infection in cystic fibrosis patients post-transplant were *P. aeruginosa* and *B. cepacia*. The latter was the major cause of death early post-transplant. With evolution in taxonomy *B. cepacia* has been reclassified as a complex divided into genomavars [Coenye T.J Clin Microbiol 2001;39:3427]. Transplant outcome varies according to genomavar with *B. cenocepacia* (genomavar III) carrying
the worst outcome [De Soyza A. Thorax 2004;59:526]. Other *Burkholderia* such as multivorans (genomavar II) or *B. gladioli* have had fewer reported complications post-transplant but the studies are so small that it is hard to generalize the results [Khan Su. Chest 1998;114:658].

*Aspergillus* which may be isolated in 40-50% of patients pre-transplant has been associated with a large spectrum of complications post-transplant; disseminated disease carries a high mortality [Helmi M. Chest;203:800; Minari A. Transpl Infect Dis. 2002;4:195].

2. **Cystic Fibrosis Related Diabetes (CFRD)** occurs in a large proportion of patients after transplant. Management differs from the conventional due to the concomitant use of medications that influence blood sugars including tacrolimus and prednisone [Hadjiliadis D. Clin Transplan 2005;19:773].

3. **Gastrointestinal complications** are not uncommon and include gastroesophageal reflux disease, delayed gastric emptying, and DIOS [Gilljam M. Chest 2003;123:37]. Liver dysfunction or cirrhosis was a contraindication for transplant in the early years of transplantation for CF. However, liver disease has in general a very slow progression post-lung transplant despite exposure to medications [Nash E. Clin Transplant. 2011]. Combined lung/liver transplant has been used for selected cases [Couetil J. J Thorac Cardiovasc Surg 1995;110:1415].

4. **Osteoporosis** affects CF patients pre transplant and invariably worsens post-transplant. It has been extensively studied in CF patients post-transplant but fortunately its effect on survival is not substantial [Tschopp O. Am J Transplant 2002;2:167; Aris R. Am J Respir Cri Care Med 2000;162:941].

**New and future challenges:** As cystic fibrosis patients are surviving longer we will see a larger number of patients with CF waiting on our transplant lists. As we transplant older patients we will also need to be aware of rare complications including coronary artery disease and microangiopathy associated with a long history of diabetes. Gastrointestinal malignancies are known to have a higher incidence in CF patients [Neglia J. N Engl J Med 1995;332:494.] and their risk may increase post-transplant due to the immunosuppression although comprehensive studies are lacking to confirm a higher relative risk. Newly identified organisms infecting these patients are being reported such as *Ralstonia, Cupriavidus, Pandoraea, Achromobacter, Inquilinus limosus, Segniliparus rugosus, Scedosporium prolificans and S. apiospermum* [LiPuma J. Clinical Microbiology Reviews.2010; 23:299. Only time will tell us their impact on transplant outcome. Despite recommendations against pregnancy by most of the transplant programs a number of CF patients have achieved a pregnancy as part of living a normal life. Fortunately, with careful evaluation and counselling most cases have had a happy ending [Gyi KM. J Cyst Fibros 2006; 5:171].

In conclusion, lung transplantation for CF patients has proved to be a challenge since it was first attempted in 1985. We have learned a great deal about how to successfully manage these patients but we need to be aware and prepare to develop special surveillance protocols for future challenges.


Was My Transplant Worth It?

Margaret A Lapsanski

In the 28 years that I have been alive, I have been asked many questions by many different people. What college would you like to go to? What is your “five year plan”? What do you want to be when you grow up? Would you like fries with that? But the question that always interests me most and invokes the most loquacious response is: “Was your transplant worth it?”

Growing up with cystic fibrosis was always a challenge. Up at night coughing made me exhausted for my daily routine of school and activities. Coughing up wads of mucous in the middle of class made me self-conscious. As a 14-year-old freshman in high school, I weighed only 80 pounds. The dreaded mile run in gym class was an event that I never could finish in the 25 minutes we had to complete it.

My parents and sister had to take on a lot for me. My sister always had to do extra chores and help me with my IV medications. My mom drove me a hot lunch to school every day in the hopes that I would eat it and gain a little bit of weight. I can’t even imagine what my father had to deal with financially. This disease had caused so many burdens.

For all of the things that could have possibly kept me down, cystic fibrosis also made me stronger. I worked harder at school, determined to leave New Jersey and go away to college to take care of myself. After my high school graduation, I was off to Lafayette College in Pennsylvania and a whole new reality. I had a great group of friends in both high school and college who cared for me, always making sure I got through the hard times. During my junior year of college, it was becoming painfully obvious that my life was slipping away from me. My friends had to help me with my laundry and carry me up the stairs after class. Instead of walking around my very small campus with my friends, I had to drive. People gave me piggy back rides when I felt I couldn’t walk anymore. Eating, dressing, showering, and combing my hair all became Sisyphean tasks.

The whole time I was going through this, my concerned family was begging me to come home from college and let them care for me. When I finally heard news in the doctor’s office that no one ever wants to hear: “You need to be on oxygen full-time,” “You have end-stage CF,” “You need a transplant if you want to survive,” I knew it was time for a drastic change to ensure my survival.

The decision for me to move to New Orleans, a place where the transplant list was shorter than in the region where I lived, was not easy. Moving away from my hometown meant moving away from my comfort zone. My family, friends, and familiar places were no longer there to provide an escape for how hard life had become. But I
also knew that my time was running out, so when the decision was made to move for the transplant, I was more than ready for it. This life felt like it was no longer mine because I was bound by the chains of losing my independence.

While I waited in New Orleans for a life-saving Bilateral Sequential Lung Transplant, I had plenty of family and friends come to visit. They kept me occupied while they were there. When no one was visiting, my mom, sister and I spent long days and nights together bonding while my dad stayed in New Jersey working hard to maintain two households. When I was by myself, I had nothing more to do but to think. To think about how I was in a very gray area of waiting to live or die. To think about how, for a majority of the population, breathing was something they never even thought about. And here I was, contemplating every labored breath my diseased lungs were taking. To think about how I was going to put one more piece of food in my mouth and still be able to take a breath of air to keep me alive.

But even through all this, I never gave up my hope and zest for life. What kept me alive were the thoughts of the possibility of going back to school and having a life where I could breathe. Imagining what it would be like to take a deep breath or sit around the kitchen table with my family laughing without having a coughing attack. This is what kept me fighting every day that I waited for that call. In the end, I was lucky since I only waited for 5 months. I got the call on November 10, 2004 around 7 in the morning.

As far as transplants go, mine was pretty uneventful. I was told that my lungs were replaced without a problem. I woke up on November 11th in the ICU surrounded by my very dedicated transplant team and remember having the breathing tube pulled out. The next couple of days will always remain hazy but I remember sitting in a chair on November 12th and being moved out of ICU on the 14th. Slowly, I started gaining my strength back. I was walking around the hallways as much as I could and for the first time, in a very long time, I walked up a flight of stairs. My family stood behind me the whole time, as they always did.

Slowly, I started to gain my life back. I had a few bumps in the road in the beginning after my transplant. There was one episode of acute rejection and two upper respiratory infections. But after living in New Orleans for 9 months, I was officially allowed to leave in March 2005.

My homecoming was spectacular. My family and friends, waiting for me to arrive in Newark airport, were all dressed up as super heroes. My cousin had hired a bag piper to give me a proper welcoming. Spiderman doing the Irish Jig in baggage claim was quite the site to see. After a warm welcome home party, I settled back into the house in which I grew up. I even made a special visit to Lafayette College where most of the campus greeted me in the student center.

After the initial homecoming, things started returning to normal. But now, all of a sudden, it was this new and wonderful normal. The chains that had bound me were gone. My independence was now mine again—all because I could breathe! I wasn’t just breathing to stay alive anymore. I was breathing so that I could live my life. All of the mundane tasks of life were now easy to do. Cooking, cleaning, and laundry were all things I could not wait to do.
Most importantly, my transplant has given me the gift of time and allowed me to do the things I had only dreamed of doing. I finished college and became employed in New York City at a major insurance company. I had a dream of working on Wall Street ever since I visited the stock exchange when I was 17 and here I was. I moved into the city with my sister into a great first apartment. I was able to take the subway to work, walk blocks upon blocks with my family and friends who always wanted to take in the sites. My new lungs allowed me the freedom to travel to great places like Las Vegas, Turks and Caicos, Mexico, the Bahamas, Texas, Florida, Aruba, California, and even skiing in Colorado and New Hampshire. There was also no greater pleasure than to learn American history by walking around Boston and Washington DC.

I’ve had the chance to watch my cousins grow up to cheerlead and play football. I have had the chance to play in the pool with them and jump on the trampoline. I have attended my friends’ weddings and been a bridesmaid seven times. Even I, the awkward girl in high school who never had a homecoming or prom date readily available, have had the chance to grow into a Natural Woman. My transplant afforded me the confidence to have fun dating which eventually led to me falling in love with the man of my dreams. All of these important events happened without being punctuated by a cough.

Of all the things that I have accomplished because of my transplant, the pinnacle was running a half marathon. The girl who needed to be carried to class and who could not walk up a flight of stairs, ran 13.1 miles. My transplant hasn’t been perfect. I’ve suffered from sinus polyps, diabetes, multiple cold viruses and a lymphoma of my esophagus. But the bottom line is, I could not have done all of these things without the generosity of my donor family, my dedicated team of physicians, and my new lungs that allow me to take a deep breath every day.

So was my transplant worth it? Yes … it was.
2012 Scientific Program Committee
Halftime Report

Stuart C Sweet, MD PhD
2012 ISHLT Scientific Program Chair

I am pleased to report that the first half of the program development is nearly complete. The efforts of the Scientific Program Committee have resulted in the Preliminary Program and Call for Abstracts Brochure, now available on the ISHLT website at http://www.ishlt.org/meetings/annualMeeting.asp.

Inside you will find detailed information regarding the plenary sessions and symposia that comprise the majority of the invited program content as well as everything needed to complete your plans to attend. Highlights include an opening plenary session that focuses on how the raising of the iron curtain has affected health care in the Czech Republic and features a keynote address from internationally acclaimed physicist, commentator and essayist Lawrence Krauss, speaking on the impact of politics on scientific advancement. I’m sure that this session will provide contemporary examples of the history, hubris and freedom themes that Dr. Valentine wrote about in September.

Another highlight will be back-to-back satellite symposia on Wednesday focusing on clinical, pathology and basic science aspects of antibody mediated rejection in heart and lung transplant. It is my hope that these sessions will provide a forum in which the October themes of collaboration, conformity and consensus will be foremost in the minds of attendees.

I am particularly looking forward to the “ISHLT Traditions” plenary session where, after registry presentations showcase some of the best collaborative efforts of our society, Professor Sharon Hunt will receive the Lifetime Achievement Award to recognize her relentless efforts to bring Heart Transplantation Medicine from its inception at Stanford to its current international excellence. I cannot think of a more fitting recipient.

I’d again like to thank all of the members who submitted ideas for invited content and particularly the members of the Scientific Program Committee who melded those ideas into what I believe will be an excellent program.

The Scientific Program Committee Executive team is now busy reviewing our second half strategy. The majority of the next steps will depend on you: the remainder of the program will showcase your work. The abstract submission site is has been open since Aug 30th - Kate Hayes from
The Alfred Hospital in Australia gets the nod for the first abstract submitted (“Effects of exercise training on exercise capacity and quality of life in patients with a left ventricular assist device (LVAD): a randomised controlled trial”). **You have until November 18th to submit your abstract.**

Please note two changes in the abstract submission process implemented this year. The first relates to Abstract Categories. In an effort to ensure that abstracts are directed to the most appropriate reviewers and attract submissions that broadly span the clinical, translational and basic science aspects of our field, we have increased the overall number of abstract categories by creating subcategories under several main categories that reflect the primary areas of interest comprising the ISHLT: Heart, Lung, MCS, Pulmonary Hypertension, Pediatrics, Nursing / Allied Health, Pathology and Basic Science. (Note: abstract subcategories for some Councils (i.e. ID and Pharmacy/Pharmacology) are distributed under other main headings.) We hope that you will find this new categorization helpful as you prepare your abstracts.

Finally, this year we are seeking abstracts in four "Topics of Emphasis". This designation is intended to attract abstracts to complement the themes of two of the plenary sessions and provide counterpoint for invited speakers in two "featured" concurrent basic science sessions. (Please see the abstract submission site instructions for details.) The “Topics of Emphasis” for the Prague meeting are:

- The aging population: Impact on treatment of heart and lung failure
- Information technology and healthcare delivery
- B-Cell basic science
- Tolerance in Thoracic Transplantation

The best abstracts in these categories will find their way into the relevant plenary sessions and the “Featured” concurrent abstract session.

I have been honored to serve as your program chair this year and look forward to the second half of the process. I am eager to review your abstracts in December and hope to see as many of you as possible in Prague!
In the beginning was the word and hence it is appropriate to consider the origins and derivations of the language we use internationally to describe graft dysfunction after lung transplantation. It may come as a surprise to a number of readers that the original recipients of heart-lung transplantation at Stanford University were cared for by our cardiac colleagues in the main and while a rigorous schedule of surveillance of the cardiac allograft was undertaken, the lungs were often relegated to the role of a support organ (the term bookends comes to mind). Specific surveillance was not undertaken. Perhaps as a result, graft failure when it occurred was misunderstood and despite open lung biopsy and post mortem examination of the allograft it was thought that the lungs were failing due to pulmonary fibrosis.

Connor Burke, who was then a Fellow in the Department of Respiratory Medicine at Stanford, was puzzled by the discrepancy between the physiological manifestation of lung allograft dysfunction, specifically an obstructive ventilatory defect and the pathological reports of fibrosis which should have caused a restrictive ventilatory defect. He discussed this with the late Charles Carrington who, to his credit, recut and reviewed the tissue blocs with Elastin van Giessen staining prior to issuing amended pathology reports which correctly identified the presence of bronchiolitis obliterans. This led to much discussion in the Department regarding nomenclature and for reasons that were deemed appropriate in those politically sensitive times, the order of the adjective and the noun were reversed and Americanized, so “bronchiolitis obliterans” became “obliterative bronchiolitis”, which had the added benefit of introducing a new acronym, OB, that was socially more acceptable than the alternative! Also, OB was preferred over BO to mark a difference between lung and non-lung transplant recipients, such as bone marrow transplants where BO had been described. Of course, the pathology is identical, or virtually, except perhaps for the origin of the effector cells being host and graft respectively.

Professor Eugene Robin, former ATS President and doyen of patient rights had coined the cumbersome acronym UUOLD in a previous publication to describe the “unexpected, unexplained obstructive lung disease” which beset the recipients of lung allografts. Thankfully, pathological insights and elegant simplicity determined that OB became the preferred terminology. Concurrently, Gary Epler had described the “new” entity of bronchiolitis obliterans organizing pneumonia or “BOOP” in a series of non-transplant cases in The New England Journal. The principal manifestation was the organizing pneumonia with secondary small airway changes; nevertheless it took almost 20 years before the term BOOP was supplanted by COP (cryptogenic organizing pneumonia) or just OP, which had in fact been described by Tony Davidson from Brompton prior to the Epler article. In the absence of a
sexy acronym (non-classical scholars will appreciate the allusion to Betty Boop and her antics) BOOP had held sway for almost 2 decades reflecting the power of words.

As the diaspora of lung transplantation grew, new units developed and provided hope that OB was “the Stanford disease” as they did not diagnose it, nor claim in a number of critical publications that they were able to prevent it by diagnosing and preventing acute cellular rejection, CMV pneumonia and PCP, nor by doing single lung transplants which were “immune” from this complication. Of course you can’t find a fever if you don’t take a temperature and in this important domain ignorance translates to a very temporary bliss. Longer term follow up has demonstrated that OB is a ubiquitous time dependent outcome after all forms of lung transplantation and in retrospect it is amusing to reflect on the supremacy of hope versus experience exposed in these publications. Accordingly, it was recognised at the ISHT Annual Scientific Meeting and Sessions (yes, International Society for Heart Transplantation, prior to the name change) that a common language was needed to allow investigators and clinicians working throughout the world in the new field of lung transplantation to describe and quantify lung allograft dysfunction. Hence the term “bronchiolitis obliterans syndrome” (BOS) was born to connote a syndrome of post lung transplant allograft dysfunction characterized by obstructive ventilatory function, recognizing the diagnostic imprecision of transbronchial lung biopsy to diagnose OB and the limited risk-benefit ratio of surgical lung biopsy, in the absence of proven effective therapies.

While the act of conception may have demonstrated a surgical swiftness, it was a difficult parturition and childhood prior to a very confusing adolescence, punctuated by multiple publications which seemed to ignore the detail of the original guidelines paper and lumped all patients with allograft dysfunction into the one box, using the terms OB and BOS interchangeably. An excellent second BOS guidelines paper by Marc Estenne et al sought to redress some of these issues and to provide a greater uniformity of description as well as identifying the predictive power of minor changes in flow-volume loop parameters as a harbinger of BOS. Now the circle is turning with the recognition of diverse phenotypes of allograft dysfunction including those which are primarily fibrotic but before we embrace new acronyms it is appropriate to be aware of the past and the potential jeopardy of using such acronyms before we have agreed on robust definitions which can be validated. For the moment, we are left with BOS, OB and OP, the latter two of which can cause chronic lung allograft dysfunction (CLAD), but that is another story!
Do We Have An Iron-CLAD Definition for Allograft Dysfunction After Lung Transplantation?

Sangeeta M Bhorade, MD
University of Chicago

What is the definition of lung allograft dysfunction after lung transplantation? Is it BOS or OB? Is it CLAD? Are there other phenotypes such as RAS? NRAD???

Currently, all these terms have been proposed in the literature as various phenotypes of allograft dysfunction after lung transplantation. However, the only established definition of chronic allograft rejection endorsed by the ISHLT is the histologically-defined obliterative bronchiolitis (OB), and its physiological surrogate, bronchiolitis obliterans syndrome (BOS), an irreversible decline in the forced expiratory volume in one second (FEV1) > 20% of baseline highest values in the absence of another known cause. The question remains as to whether BOS/OB sufficiently explains with clarity and precision our growing knowledge of chronic lung allograft rejection.

The controversy arises from our inability to identify a single patho-physiological mechanism by which lung transplant recipients lose their lung function, leaving us with no medical alternative to improve survival in patients with end stage BOS other than re-transplantation. In addition, it is difficult to predict which patients will have a more rapid and progressive trajectory of decline of their disease compared to those who tend to have a slower decline and in some instances stabilize their pulmonary function. As a result, there is increasing consideration that chronic allograft rejection may be a heterogeneous disease with several phenotypes, of which BOS may be merely one.

Chronic lung allograft dysfunction or CLAD has recently been documented sporadically in the literature as a more comprehensive definition of the persistent decline in lung function after lung transplantation. In these studies, CLAD, a poorly standardized term, appears to be inclusive of several different conditions that may lead to a decline in pulmonary function. For example, the following conditions have been included within the definition of CLAD: the presence of BAL neutrophilia, (neutrophilic reversible allograft dysfunction), the presence of various histological findings (follicular bronchiolitis, DAD, interstitial fibrosis), the presence of several radiographic patterns (upper lobe fibrosis, parenchymal infiltrates, pleural disease, mosaicism, etc.) and the presence of restrictive physiology (restrictive allograft syndrome (RAS), restrictive BOS (RBOS).

So, does the term “CLAD” clarify and add precision to our current understanding of allograft dysfunction or does it simply disguise the issue by adding yet another name? In lung transplantation, we are becoming more aware of the nuances of the progression of “allograft dysfunction”. Most transplant physicians agree that chronic rejection is a multifactorial, heterogeneous disease process. Does “splitting” these categories into the various subtypes under the global term, CLAD, truly elucidate our understanding of this complex disease process?
Some argue that it enhances our knowledge regarding potential pathophysiological mechanisms that ultimately lead to chronic allograft rejection and allows us to consider individual therapies for each of these subtypes (ie azithromycin for NRAD). The counter argument in identifying these different phenotypes under the umbrella of “CLAD” is that these phenotypes have been identified retrospectively in small single center studies and have not been validated yet in larger prospective multicenter cohorts. As a result, our knowledge of these phenotypes remains unclear. Are these phenotypes part of the spectrum of the same disease process? Are these distinct phenotypes or is there a significant overlap among these phenotypes? Is BOS/OB the final common pathway of multiple insults/injury to the allograft? The addition of new terminology, such as CLAD, and the other new acronyms may simply add jargon that distracts us from truly focusing on understanding this disease process.

As a transplant community, we have come a long way in understanding the complexities of chronic allograft rejection! Several of the newly described phenotypes that are defined by different pathophysiological mechanisms appear to respond differently to individual therapies. However, the lung transplant community has not officially addressed whether CLAD is the appropriate global term for lung dysfunction and if accepted, how CLAD should be defined. Is it time for a new consensus panel to determine whether chronic lung allograft rejection should be “CLAD” with a precise definition? Keep in mind the concept Roger Evans alluded to in the August Issue of the Links: are we in a “generation gap” where new words are substituted for old well-worn concepts as a result of expecting something from nothing? Will this Iron-CLAD change provide better precision and clarity and would a rose by any other name smell as sweet?
Lung Re-Transplantation – or Not?

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Newcastle University, Freeman Hospital

Most, if not all, lung transplants will eventually fail, and we tell this to our patients as they are listed. “What happens then, Doc? Do I get another?”

“Unlikely,” is the honest answer, but providers of lung transplantation remain undecided. There are two sides to the argument, one put here by Dr Pessimist, a pulmonologist with bow tie and thinning hair. The opposing view comes from Dr Optimist, a surgeon; big man, drives a red Porsche.

“Why don’t you send more of our patients up for another graft?” questions Dr O. “Enough of them are dying late, under your care, despite all my efforts to give them a good graft.”

“The Results are bad” is the response. “We have more than enough patients on our waiting list, some of them die every year. We don’t have enough lungs for the ones we select well, so why add to their numbers with re-transplants? It’s a cruel world; each person has just one chance. And the surgery is difficult....”

“But are the results that bad? Several studies have shown progressive improvements, particularly in the past decade. The annual number of retransplants in the ISHLT Registry has more than doubled in the recent era. This has been driven by LAS in the US with similar optimism in Europe. Major centres like Vienna and Hannover report substantial series.”

“OK, OK, but they are still worse than the standard, first time transplants. We have to do the most benefit with our small donor pool. We owe it to everyone on the list, we owe it to the families of donors, to get the best result.”

“True, but look at the details. Across the board the hazard ratio compared with first timers is 1.1 – 1.3. Worse, but no more so than for patients with pulmonary hypertension, sarcoid or a CF with pan-resistant colonization. We accept them, after careful thought, but they still get listed.

“And there are subsets within the re-transplantation group who clearly do less well. Early re-transplantation most often for primary graft dysfunction is not a good idea. Even worse as a solution for acute rejection. These are old lessons, and should not be re-learned. Similarly renal failure is bad news. If we exclude them, results begin to look comparable.
“Finally, let me deal with the technical difficulties....”

We are left, then, with a problem that has both ethical and practical dimensions. There will be substantial numbers of patients with graft failure in the mid-term, patients who are still young and otherwise well. If judged by widely adopted acceptance criteria, they should be listed for re-transplant. They have the advantage of living with a transplant, of already having gone through the procedure. Their compliance is already tested, in contrast with many on our waiting lists. Surgical difficulties undoubtedly exist, but in many cases they are no worse than for first time operations and may be better. Previous suture lines show the surgeon where to cut and the pleural adhesions, perhaps because of post-op steroids the first time around, are often modest. The locked-in lung of a patient with LAM and a pleurectomy is always more challenging, but we list them with little hesitation.

Within our Utilitarian philosophy, wanting to do the most good for the most people, these patients should not be denied another chance. We should temper our enthusiasm for the ventilated recipient, or the established renal failure. We should not let long-term familiarity with a patient treated over many years interfere with the objective judgment of the team. Within that same philosophy, it is only fair to apply the same criteria as our first-time transplants.

History supports this view – we are doing more re-transplants, with better results, in all the major transplant centres. These patients deserve our best efforts.

NB
These arguments are set out in much greater detail, and with good scientific analysis of the data, in papers by Steven Kawut, most recently “Lung Retransplantation” Clinics in Chest Medicine 2011; 32:367-77.
The Second Time Around

Delaine Jarreau

Even after being diagnosed with Cystic Fibrosis at age 7, I have been a very active person, playing basketball and softball most of my life. I think because I didn't have serious lung issues until I was in my 20’s, I really never thought about the disease being life threatening. In 1997 as my lungs worsened, I was basically told that my only hope was lung transplantation.

In 1998, I was placed on the transplant waiting list at Ochsner Hospital in New Orleans, Louisiana. My doctor was straight to the point, telling me this is no cake walk and giving me all the statistics. Many people had told me the same thing over and over: “You are trading one set of problems for another”. That statement always seemed strange to me because when one’s option is death, one can deal with anything including many problems.

When the time finally came it was not a moment too soon, as many people said I would not have made it another week. On February 9th, 1999 at age 30 I had a double lung transplant at Ochsner Hospital.

I do not think there is anything in the world that can prepare your family for the way you look right after the surgery. There are so many hoses, wires and machines attached to your body that your family can hardly recognize you. Honestly the next few weeks were probably harder on my family than me. The hardest part of it all for me was the ventilator. I hated that thing with a passion and could not wait to get off of it. I remember my first breath without it was a remarkable feeling. Since my diaphragm was not working properly, I could not take a deep breath and still needed oxygen, but wow—I could tell the difference immediately, it was still an improvement, weak diaphragm and all.

Over the next several weeks, I faced several problems. A bronchoscope revealed that my lungs were working but had been “burnt” from being outside the body too long, causing them to shed or peel almost like after a bad sun burn. I was assured this would get better. After about 3 months I was back at work and resuming a normal life.

To this day I have continued to wonder about what I had been told about trading one set of problems for another. The problems I had now were not stopping me from living a normal life, which is all I wanted. Most people with CF know how much time you have to spend each day doing the things that keep you breathing. Now all I had to do was swallow pills and workout. Wow—I could take those problems any day over all the other things I used to have to do.
The next two years I truly enjoyed life. My husband, Travis, and I traveled, camped, fished and worked out together. For the first time in a long time, my ‘normal’ life allowed me to feel like a Natural Woman. I remember clearly the difficulty my mom had adjusting to letting me do my own housework. I had to tell her to stop coming over—that I could do my own clothes and house work now. Things could not have been any better until ....

A very slow process had begun and my lungs began to reject. My doctor tried everything to stop the process but knew that it was only going to get worse. At that time, I was truly in the best shape of my life so my doctor spoke to me about having another transplant. The memories of what I had to go through with the first transplant made me think twice about choosing to go through it again. These second thoughts were not about me—they were about my family. The thought of having to put them through the transplant process again is what really caused me to second guess. After my family eased my mind that it was worth it to try again, I told my doctor to list me again on the transplant list. Two weeks later I got the call.

I must say the second time around was not any easier. Again I had trouble with my diaphragm not working and had to stay on the ventilator longer, causing me to undergo a tracheotomy, especially needing it when I laid flat. Even as I write this, I am struck by the things I don’t remember, things my husband is telling me that I had totally forgotten. It has been nine years since my second transplant and life has been so great that I think the human mind tends to suppress the bad stuff. About two months after my second transplant I was off the vent, back at home and at work.

Today, it is amusing to me that the problems I have are ‘normal’ ones, like being told, “Delaine, you need to lose weight and work out more.” All my life I have searched for ‘normalcy.’ Although I still have to do some things that are not completely normal, at least now my problems are manageable. I am gainfully employed full-time and a very active person. I have even done some things that I think have given my mom a heart attack, like riding a motorcycle in the Tennessee Mountains and wrecking—with the bike landing on me. The ER doc said I had nine lives for sure.

We certainly never know what the outcome is going to be when we have disease in our life, but I think having a transplant is certainly a viable option for anyone who has no other option. The second time around was definitely a charm for me and I thank God every day for giving me a second chance. I realize that this may not be forever and things can always change in the blink of an eye, but I will continue to live life like tomorrow is not certain and enjoy my time here.

I am very thankful that my doctor talked me into doing a second transplant and for the team of doctors who keep me going now. I am thankful to all the staff at Ochsner and UTMB. A special thanks to Giselle, Denise and Stephanie for putting up with me all these years. All of you have been such a blessing to me and I could not have gone through all of this without you.
Quality of Life in Lung Transplantation – Why is it Important?

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As lung transplant specialists we believe we are in the business of saving lives – come to think of it, we are. Every day, we have the privilege of witnessing desperately ill patients – on the inexorable downward slide of pulmonary fibrosis or on extracorporeal support for end-stage cystic fibrosis, for example - brought forth from certain death to a second chance at life.

However, we list and transplant many patients whose death is less certain. Recent modeling studies indicate that many lung transplants do not confer an expected survival benefit (Thabut et al, AJRCCM 2008;177:1156-63; Liou et al, JAMA 2001;286:2683-2689). The advent of the Lung Allocation Score has improved waiting list survival, but perhaps at the expense of post-transplant survival (Merlo et al, J Heart Lung Transplant 2009;28:769-75). This is not unique to lung transplantation; for example, similar analyses have been reported for heart and liver transplantation (Deng, MC et al. BMJ 2000;321:540-545; Merion et al, Am J Transplant 2005;5,307-313).

Are these transplants misguided? A waste of organs? Or evidence that clinicians and patients implicitly recognize improvement in quality of life as an important indication for organ transplantation? We have all seen patients who suffer terribly from dyspnea, disability and social isolation without any clear prognostic indicators to favor transplantation. Perhaps transplantation is justified if it improves quality of life, or especially quality-adjusted survival, in such patients. For example, our group has found that the quality of life benefit in the first year after transplantation is similar for emphysema patients with a BODE index of 5-6 as for those with a BODE index of 7-10 (Eskander et al, J Heart Lung Transplant 2011:online July 22, 2011). We have also shown that the LAS, designed to predict survival, does not necessarily correlate well with quality of life measures (Gurau et al, J Heart Lung Transplant 2007;26:S160). However, we currently have little understanding of the clinical factors that predict a quality-adjusted survival benefit of transplantation.

Some also wonder about the quality of life outcomes of lung transplantation for the desperately ill whose lives we are saving with transplantation. These patients often have a more difficult recovery complicated by critical illness neuropathy/myopathy, renal failure, hospital-acquired infections, and cardiovascular complications, just to name a few. We need to understand the quality of life experienced by these patients to have a complete picture of the risks and benefits of transplantation.

Many members of the Pulmonary Scientific Council are interested in exploring these issues, and we have formed a Workforce to foster dialogue and collaborations. This group includes dozens of participants from North America,
Europe, Asia and Australia. Our first research initiative is a multicenter pilot study titled QUILT—Quality of Life in Lung Transplantation. Our plan is to collect longitudinal quality of life data though a web-based interface, which will be linked to the ISHLT Registry for correlation with clinical data. We hope to expand beyond this small pilot group to include all centers reporting to the Registry. Many workforce members are also engaged in individual research projects and benefit from the sharing of ideas and experiences.

As we seek to better understand the influence of transplantation on quality of life, what can clinicians do to optimize quality of life for our transplant patients? Ask transplant candidates about the effect their lung disease has on their quality of life, and how they envision this being improved by transplantation. Check back regularly after transplant to ensure that these goals are being met. Some clinics use direct quality of life measurements to enhance these discussions (Santana MJ et al, Qual Life Res 2010;19:371-9). Think before telling a patient they 
\textbf{can’t} (travel, garden, own a pet, work in a crowded environment, become a parent, etc.) – are you doing all you can to help this person safely attain their life goals and enhance their quality of life? And don’t overlook the quality of life of patients on the waiting list or with late-stage chronic allograft dysfunction – compassionate, attentive and sound palliative care is the important treatment you can provide.
Another of the core disciplines at the foundation of our society, management of respiratory failure and pulmonary replacement therapy, will be prominent topics throughout the meeting. In addition to the pulmonary aspects of antibody mediated rejection to be included in the pre-meeting AMR sessions, the first pre-meeting symposium devoted to lung transplantation, Evolving Concepts Of Chronic Lung Allograft Dysfunction, will review new concepts of chronic lung allograft dysfunction and will reflect some of the conclusions and recommendations reached by the joint ISHLT/ATS/ERS task force on care of the lung transplant recipient. Advances In Pulmonary Transplant Surgery, another pre-meeting symposium, will include presentations on airway complications, mechanical bridging and ex-vivo lung perfusion.

Concurrent symposia on Thursday and Friday include the session, Special Considerations: Cystic Fibrosis and Lung Transplantation, which will review the complicated microbiology, surgical considerations and psychosocial issues associated with transplant of the CF patient. An international review of Lung Transplantation for Pulmonary Arterial Hypertension will focus on the impact that regional variability in listing status, organ allocation and the type of organ transplantation have on outcomes, and finally a session on Challenges in Pediatric Lung Transplant that will close with a presentation on transition of the pediatric lung transplant recipient to adult care.

Glasgow, UK: Congratulations to ISHLT member, Dr. Carla Baan, who became the 15th president and first transplant immunologist president of ESOT during its annual meeting and scientific sessions held in Glasgow in early September. Dr. Baan, a native of the Netherlands, received her PhD from Erasmus University, Rotterdam, The Netherlands, in 1998 with her PhD thesis focused on intragraft cytokine mRNA expression after clinical organ transplantation. She has been a member of the faculty of Erasmus University since that time, currently serving as Associate Professor and Head of the Laboratory for Nephrology and Transplantation. In 2009 she was a visiting professor at the National Institute of Arthritis, Musculoskeletal, and Skin Diseases at the NIH, Bethesda, MD under Dr. John J. Shea. Dr Carla Baan’s research interest focuses on the role of cytokines, regulatory T cells, mesenchymal stem cells and immunosuppressive drugs in clinical organ transplantation. The aim of this translational work is to titrate the immunosuppressive burden in our patients in such a way that side-effects (infections, malignancies, cardiovascular events) are kept at a minimum while at the same time rejection processes are prevented.

Dr. Baan’s goals for ESOT during her tenure as president, as outlined in her Presidential Address, include;
1. To bring down barriers between basic scientists and clinicians by promoting research;
2. To expand education and outreach; and
3. To create an interactive platform for the student and young professional members of ESOT.

Dr. Baan was instrumental in the development of a joint ESOT / ISHLT session to be held at the ISHLT Annual Meeting in Prague in April, 2012. The session, slated to be chaired by Dr. Rutger Ploeg from ESOT and Dr. David Taylor from the ISHLT, will include talks on the following topics:
1. The impact of DCD donors for thoracic donation;
2. Are Tregs ready for the clinic? (to be presented by Dr. Baan);
3. Clinical experience with Belatacept: A Balanced View; and
4. The impact of ABO incompatibility on de novo HLA antibody production.

Please join me in congratulating Dr. Baan on her role as the new leader of ESOT – and plan to congratulate her in person when you attend the ESOT / ISHLT Joint Symposium session in Prague.
5th Prague Adventure of Mr/s XYZ at ISHLT 2012: The Land of Dumplings, Sauces, and Sweet Entrees

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It is lunchtime and you have returned to the cafeteria-style restaurant in center-Prague to taste yet another Czech specialty. You decide on guláš (pronounced gulas) today. You successfully navigate the long counter with your food tray, managing to obtain the correct guláš soup and then the guláš main course with a Gambrinus beer. You are now sitting at a long wooden table opposite two young businessmen who are having a lively discussion in Czech. You admire the plate in front of you with a heap of dumplings and an orange beef stew. Two middle-aged ladies bring their food trays over and sit beside you. You find the seating arrangement somewhat comical, reminiscent of your school cafeteria or perhaps your Boy Scout summer camp.

Among your all-time favorite activities—somewhere up there with traveling—definitely is eating. So what could be better than eating while traveling? You have been well warned by your Czech friend back home: #1, don’t try to be on a diet in Prague; #2, Czech food and healthy food are polar opposites; #3, the most authentic Czech food is usually served in little local pubs and not in big fancy restaurants.

Given your food fetish, you have been keeping a “mental food diary” since your arrival to Prague. You have tried several pubs around the conference center and a few cafeteria-style restaurants in center Prague. You now have accumulated a wealth of key observations about the Czech culinary world:

Knedlíky - this is the Czech word for dumplings. The Czech Republic should really be called “the land of dumplings”. Seriously, there are dozens of different kinds of knedlíky. The most common ones are bread dumplings (houskové knedlíky). They might as well nickname them “bread on steroids” since they are made of bread with the addition of flour and eggs. Then there are potato dumplings—potatoes on steroids—made of potatoes with the addition of flour and eggs. And then there are bacon dumplings—yes, you guessed right—bacon on steroids! Made of bacon, flour, and eggs, you begin to think that maybe these should be officially outlawed. Dumplings form the accompaniment food for a variety of meats. And in case there isn’t enough fat in the concoction, the meat and knedlíky get covered with a creamy sauce of some sort. We will get to that in a little bit but for now, we will keep going down the list of dumplings. Next on the list are sweet dumplings made with a variety of different dough and filled with fruit such as plums, apricots, or strawberries. And finally, there are “knedlicky”, which are “little dumplings”. These can be made of flour or liver pâté and added into soups.

The most revered staple foods in the Czech Republic include:
Vepřo-knedlo-zelo: pork-dumpling-sauerkraut
Řízek: that’s Czech for Wienerschnitzel, a large fried tender pork fillet covered in batter and breadcrumbs, usually served with potatoes, mashed potato, or potato salad
Guláš: beef stew with paprika sauce served with bread dumplings
Segedínský guláš: beef stew with sauerkraut-based sauce, usually served with bread dumplings
Poultry, such as goose or duck, with knedlíky and sauerkraut
And then a variety of meals that include roasted pork or beef with knedliky, covered with creamy gravy such as “svičková” (a creamy vegetable sauce)

Sweet entrees—now, this is interesting. You really thought you messed up and ordered dessert, but upon some detective work, you discover that Czech people really do consider these meals main courses. These include those fruit dumplings described above, plus “buchtíčky se šodů” which are little pastries that taste and look a little like Dunkin Donut munchkins covered with a sweet custard-like sauce, and “palačinky” or soft crepes filled with jam.

Then there are the real desserts such as koláče, buchty, and bábovka. They often contain interesting fillings such as milled poppy seeds, plum butter, or cottage cheese.

And then there is Czech street food (the Prague equivalent of fast food, you figured). This food can be purchased from little stands along streets and squares, including:
- Párek v rohlíku: sort of a hot dog, except that the dog is actually inserted into a hole skillfully drilled into the bun.
- Klobása: spicy sausage with bread and mustard.
- Bramborák: potato pancake or, really, another version of potatoes on steroids made of potato, garlic, flour, spices, and fried to perfection.
- Smažený sýr or smažák: grilled cheese covered with batter and breadcrumbs.
- Utopenec: a pickled sausage (but translated means “drowned person”).

Throughout your stay in Prague, in an attempt to maintain your cholesterol levels in some sort of reasonable range, you do have to intersperse the meals described above with salads from non-authentic or vegetarian restaurants that you find nearby. The excursion into the Czech culinary world helps you understand why your Czech friend laughed so hard at your pervasive broccoli, asparagus, and salads upon his arrival to your town. It has also taken this trip for you to actually believe his story about eating lard sandwiches at school as a kid (yes, apparently his mother would prepare two slices of dark bread with pork lard and salt between the two of them). Your friend did acknowledge, nevertheless, that most contemporary Czech families have increased their vegetable intake and have modified their diet away from the traditional high-fat authentic Czech food. Many families now reserve this food for special occasions and holidays, such as Posvícení, the Czech equivalent of Thanksgiving, at the end of the harvest season in early September. But already you have decided that during your trip to Prague—for you—it will be Thanksgiving every day.