IN THE SPOTLIGHT: 2016 Recipients of the ISHLT Leach-Abramson-Imhoff Links Travel Awards

Over the past year, the ISHLT again was very fortunate to have nearly 100 writers contributing to the ISHLT Links Newsletter. Attention to appropriate treatment strategies and drug monitoring for nontuberculous mycobacterial and fungal infections in our patients can contribute to better outcomes. Although expensive, innovative CFTR modulator therapies in cystic fibrosis continue to help patients suffering with cystic fibrosis and delay deterioration in their lung function. The dreaded clot through the heart in patients with LVAD compels us to fine tune our prevention and treatment anticoagulation strategies in this rapidly growing population. With the swift pace of innovation and focus on what’s best for our patients we need to keep our senses and sensibilities, address our own confessions especially in terms of blame yet recognize that life is not fair as we keep asking ourselves, who has time to be still? This year’s Writer of the Year Award goes to none other than Kyle Dawson. Our First Runner-Ups are Adam Cochrane and Christa Kirk, and Honorable Mention awards go to Angela Velleca and Erin Wells.

Let's extend a warm ISHLT congratulations to these writers.

**Writer of the Year: $2,500**

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Although this year’s winner is not in the heart of Texas like last year’s winner, Pam Combs, instead Kyle Dawson is a clinical pharmacy specialist for the lung and heart transplant services at Houston Methodist in Houston, TX. His role is paramount in assisting heart and lung transplant specialists with managing complex medical regimens including the festering problem of nontuberculous mycobacteria infections. His article on Pharmacotherapy Considerations for Agents Used in the Treatment of Non-Tuberculosis Mycobacterial Infections in Cardiothoracic Transplant Recipients earned him this award. In the past, he co-authored an article for the ISHLT Links, Carbapenem’s Role in Empiric and Directed Therapy for Bacterial Infections in Cardiothoracic Transplantation: Are All Carbapenem’s Created Equal? He has been a member of the ISHLT Council of Pharmacy and Pharmacology for over 5 years and is this council’s representative for the Education Committee. He is also a member of the Infectious Disease and Pulmonary Transplantation Council. He has also recently secured a Master’s in Business Administration which will be an added bonus for his career and the ISHLT.

**First Runner-Ups: $1,000**
Adam Cochrane, PharmD, BCPS  
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Another Pharmacist claims another Links Award, Adam Cochrane. He is part of the INOVA Advanced Lung Disease and Transplant Program where he serves as the Clinical Transplant Pharmacist Specialist, a key member of an outstanding transplant team. Today, he is Vice-Chair of the Pharmacy and Pharmacology Council and has been an active member of the ISHLT for years. He is a member of all Councils, except the Pediatric, Pathology, Basic and Translational, and Junior Faculty and Trainees Councils. His article on Antifungal Therapeutic Drug Monitoring: Confessions of a Pharmacist is an insightful and important article about drug monitoring in our patients. He also provided an update on the Links on Orkambi™ For Cystic Fibrosis Before and After Lung Transplantation and in the past he gave us a summary on CMV and Thoracic Transplantation.

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Yet is another Clinical Pharmacist claiming another runner-up Links Award. Christa Kirk is a Critical Care Pharmacist at Seattle Children’s Hospital and in her first article for the Links, a Clot Through the Heart...And You're to Blame? proved to be insightful, creative and exactly what the ISHLT Links Newsletter expected. Of course, referencing Bon Jovi’s “Shot through the Heart” didn’t hurt.

Honorable Mention (2 recipients): $500

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Our two honorable mentions are nurse coordinators. Angela Velleca comes from the Cedars-Sinai Heart Transplant Program as one of the lead coordinators. She has been part of the ISHLT for years and is an active member of the Nursing, Health Science and Allied Health Council. Her article on Sense and Sensibilities: Finding Consensus in Adult Cardiothoracic Transplant Nursing alluding to Jane Austen, is the result of a consensus reached in an effort to better elucidate the staffing levels and models of care from the time honored importance of nurse coordinators for heart failure, lung failure, and recipients of heart and replacement therapies.

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Erin Wells, a Care Manager of Cincinnati Children’s Lung Transplant Pediatric Team, is now a repeat recipient of the Links Travel Award in the category of honorable mention. Last year, we learned lessons from her article Lessons Learned. This year she delivered another clear and concise essay on Life Is Not Fair. She also provided us with another article Who Has Time To Be Still?

Congratulations on your honorable mention award for two years in a row.

History of the Leach-Abramson-Imhoff Links Travel Awards

The ISHLT Leach-Abramson-Imhoff Links Travel Awards, funded in part by the generous support from W.O. and Joan Leach (Gadsden, Alabama, USA), Mrs. Sue Abramson (Birmingham, Alabama, USA) and Mr. Larry Imhoff (La Place, Louisiana, USA), were created to support the growth and development of our future leaders from within our society including physicians, nurses, and other health care professionals. Those motivated enough with investigation, communication, and dissemination of new ideas for the betterment of patients with failing lungs and/or a failing heart including such conditions as pulmonary fibrosis, cystic fibrosis, emphysema, pulmonary hypertension, and from ischemic, nonischemic to congenital heart diseases should be awarded for their efforts.

Eligibility requirements include:

1. Any healthcare professional including but not limited to nurses, nurse coordinators, social workers, pharmacists, therapists, dietitians and early career physicians are eligible and must be a member of the ISHLT regardless of duration in their career.
2. An imposed restriction on physicians is that they must be in their Early Career—within 7 years of training, Assistant Professor equivalent, or junior faculty level with rare exceptions.
3. Individuals must display some form of research interest, basic, clinical, translational or outcomes investigations or at a minimum display some skill in journalism best exemplified by their contributions to the Links Newsletter engendering fresh and creative ideas.

Each year, the winners are selected from a pool of nominees by the ISHLT Links Travel Award Committee (LTAC). This committee includes the following individuals: the Links Editor-in-Chief, ISHLT Executive Director, ISHLT President, ISHLT Program Chair, and the Links Managing Editor.
Recent Progress in the Pathology of AMR and CAV

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At times, the rapid pace of new developments can be overwhelming to the practicing physician, and this is certainly true in the field of heart and lung transplantation pathology! In the November 2015 issue of Links, our Council highlighted many of the key pathology publications from the last year, to help busy pathologists stay abreast of our rapidly evolving field. But time flies even faster, as we all know, necessitating another ISHLT Links update from the Pathology Council.

In the last 3 months since our last update, we’ve already seen several new studies published that advance our understanding of allograft pathology. As in recent years, antibody-mediated rejection (AMR) and cardiac allograft vasculopathy (CAV) remain a strong focus of our Council’s discussions and research efforts. If you missed the November update, it might be worth checking out too, for a more extensive review of our field’s recent progress. In the present update, only 2 very recent papers will be highlighted that are likely of broadest interest, but this is certainly an incomplete list and many others are deserving of review, too.

Progress in Pulmonary AMR

Despite being a focus of intense interest and investigation, pulmonary AMR and its pathologic characteristics remain poorly understood. As you all know, in an effort to focus research efforts in pulmonary AMR, the Pathology Council published a summary statement in 2012 with recommendations for pathologic evaluation of AMR, which included suggestions for protocol biopsies and serologic evaluation for DSA, in order to accumulate data and begin to unravel the details of the pathology of this phenomenon.

This data is finally beginning to emerge, spurred on by efforts of our Council members and others. In January, Dr. Wallace and colleagues published a blinded multi-institutional study investigating pathologic changes in a large number of lung allograft biopsies, to see whether any statistically significant findings correlate with the presence of DSAs (http://www.ncbi.nlm.nih.gov/pubmed/26601715). They found that capillary inflammation, acute lung injury, and endotheliitis each correlate significantly with the presence of DSAs. On the other hand, they observed no significant correlation between the presence of staining for C4d and the presence of DSAs, reaffirming what many of us have experienced with our C4d stains, and again suggesting that C4d is of limited utility in the pathologic evaluation of the lung allograft.

Certainly, the story of pulmonary AMR is not over, as the transbronchial biopsy remains an imperfect tool, fraught with numerous technical and interpretive challenges, and additional studies and advances in technology are sorely needed. Perhaps the cryobiopsy will begin to shed light on this...
vexing problem as it becomes more widely adopted. In any case, we can expect a lively discussion on the topic in Washington next month!

Progress in CAV
Data on cardiac AMR and CAV continues to accumulate, but the nature of the association between cardiac AMR and the eventual development of CAV remains poorly understood, and this potential link continues to be hotly debated.

In January, Dr. Loupy and colleagues in France reported their findings in an interesting multi-center study of late failing cardiac allografts, where they investigated the pathology of CAV and its association with AMR (http://www.ncbi.nlm.nih.gov/pubmed/26588356). They also correlated these findings with endomyocardial biopsies obtained between allograft implantation and explantation. In their study, they observed evidence of antibody-mediated injury in 62% of allografts with pure arteriosclerosis or mixed arteriosclerosis and atherosclerosis, but not in allografts with pure atherosclerosis only. The authors concluded that AMR is operating in a substantial fraction of failing cardiac allografts, and is associated with severe coronary arteriosclerosis, the histologic hallmark of CAV.

This study adds to the growing body of indirect evidence suggesting a causal link between cardiac AMR and CAV. Nevertheless, much remains to be learned about the pathogenesis, tempo, and treatment of CAV, and its relationship to cardiac AMR. Don’t miss the stimulating discussions on this topic that will certainly occur at the Annual Meeting next month!

2016 Annual Meeting & Scientific Sessions in Washington, DC.
Please join us for the following pathology-oriented sessions in Washington:

Unraveling “Chronic Rejection” in the Heart, where the controversy and ambiguity surrounding chronic rejection in the heart will be discussed. What does “chronic” really mean? And are the changes we observe truly rejection? Speakers will address the myocardial alterations (beyond CAV) seen after years of repetitive rejection episodes, novel mechanisms of CAV development, the role of complement and other mechanisms in potentiating late graft damage, analogues of chronic rejection in other organs, and animal models of late graft loss.

Controversies in Heart Transplantation: Past, Present and Future, where the current status of rejection surveillance and utility of endomyocardial biopsy will be hotly debated.

Big Data to Answer Big Questions: Biobanking to “Omics” to Personalized Medicine in Thoracic Organ Transplantation, where renowned investigators will discuss the process of biobanking and proper utilization of banked specimens for research, and the promise of Big Data as a tool that will revolutionize future clinical practice.

A 2016 Focused Update on AMR in Cardiac Transplantation: Immunologic Diagnostics and the Treatment of Refractory AMR, where the current state of cardiac AMR will be addressed,
including a discussion of endomyocardial biopsy features in AMR and emerging molecular technologies for detection of AMR.

**Endotypes of CLAD and Novel Treatment Strategies**, where our current understanding of the different CLAD phenotypes will be reviewed, including their clinical diagnosis, radiology, pathology, prognosis, and treatment.

For more details about these and other exciting symposia, please visit the 2016 Preliminary Program at [http://www.ishlt.org/meetings/annualMeeting.asp](http://www.ishlt.org/meetings/annualMeeting.asp).

See you all soon!

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Life and Lung Transplantation in the Washington Area

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The Lung Transplantation community in the Maryland-Washington DC is exemplified by a spirit of collaboration among regional Transplant organizations and physicians on behalf of patients with Advanced Lung Disease.

The University of Maryland Medical Center and Johns Hopkins Hospital recently joined forces as an approved Care Center Network (CCN) site for the Pulmonary Fibrosis Foundation. “The joint collaborative CCN site allows for an even more robust multi-disciplinary approach, taking advantage of each institution’s unique areas of expertise to advance the care of individual patients, and to hopefully advance overall understanding of pulmonary fibrosis syndromes”, explained Dr. Nevins Todd co-director of the program.

Along the same lines, in the research arena, the advent of the NIH consortium is a new model for the collaborative bench to bedside research in heart and lung transplantation. Multiple programs in the region have joined this initiative and some of the preliminary findings of this joint effort will be featured at the ISHLT meeting in April 2016.

As junior faculty at the University of Maryland Lung Transplant, it has been privilege to work with my team, a group with a long history of challenging traditional concepts of lung transplant. We serve as the epicenter for the Multicenter Normothermic Ex Vivo Lung Perfusion NOVELL Trial and have one of the largest ECMO (extracorporeal membrane oxygenation) groups in the nation. In 2014, the Lung Rescue Unit (LRU) was established at our Shock Trauma Center to service the needs of patients dying from Advanced Lung Disease, ARDS, or those requiring ECMO bridge to transplantation in our region. We have the capability to triage and transport extremely sick patients within Maryland and beyond state borders, and provide lung transplantation effectively with short wait-list times and superior one year lung transplant survival. Over the next few years our team will focus on building outreach programs that provide transplant care to patients at geographic disadvantage in our State through telemedicine and tele-monitoring.

As you see, collaboration is at the core of the programs in this region.

As far as the unique features of living and working in the Washington DC –Baltimore area, to quote Dan brown, the author of the Da Vinci Code, "Washington, D.C., has everything that Rome, Paris and London have in the way of great architecture - great power bases. Washington has obelisks and pyramids and underground tunnels and great art and a whole shadow world that we really don't see.” In no other region of our country are the issues of our Nation so intimately reflected in the fabric--and traffic patterns--of our daily lives. It is a region rich with history, diversity, and culture. Every weekend adventure in DC can be catered to your varied interests with diverse museum tours,
monuments, shows, grand festivals, live music, divine restaurants and dance floors. Inevitable during your adventures, you will be greeted by reminders of the events of American history, and the forefathers, soldiers, leaders and famous/infamous characters that have crossed the same thresholds. Spending five quiet minutes in the Lincoln Memorial is a very profound American experience that I highly recommend.

Personally as a lifetime New Yorker adopting a new hometown in Baltimore, I also encourage you to experience Baltimore’s beautiful waterfronts, boat shows/events, street festivals, exhilarating sporting and music events, and renegade art scenes. The issues affecting our urban communities are palpable in everything that is Baltimore. This, as much as all the historic sites and scenic backdrops, is part of our fascinating changing identity. The growth and development of our city has been happening in leaps and bounds.

We look forward to sharing our community with our ISHLT colleagues and guests in April 2016.

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Lung Donation After Circulatory Death And The Potential Role Of Ex Vivo Lung Perfusion

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Worldwide, lung transplantation is growing and our collective outcomes are improving. These improvements are a culmination of our collective advances in patient selection, preoperative management, surgical experience, and meticulous postoperative and longitudinal care. Further increases in our ability to offer this life-giving therapy to patients in need is, and will be, limited by the availability of numbers of donors of sufficient quality. In order to meet the demand, non-traditional (i.e., brain-dead donors (DBD)), approaches need to be pursued. Lung donation after circulatory death (DCD) is one potential avenue. Although this approach may provide the ability for more people who wish to be an organ donor to be an organ donor there is some trepidation on the part of transplant programs to venture into this area because of concerns of potential risks [1]. The concomitant, more widespread adoption of ex-vivo lung perfusion (EVLP) may allow for the management of that potential risk, the assessment of the DCD lung donor, and enhanced recovery.

The International Society for Heart and Lung Transplantation (IISHLT) has supported the development of a DCD Registry [1,2]. Recently, this registry was evaluated and data from 10 participating institutions in North America, Europe, and Australia was analyzed. In these centers, 306 DCD donor lung transplants were performed. The vast majority were Maastricht Category III recoveries. These donors were compared to an almost 10-fold larger DBD donor cohort. The 30-day and 1-year survival between these donor cohorts were not different [2].

These types of data are increasing and demonstrate that the approach to DCD lung donation can occur. However, the underlying theme that is being further elucidated is the deliberate programmatic approach to the success attained at these centers. Examples of these approaches are standardization as much as possible in heparinization, withdrawal of life support, donor extubation, recovery technique, and the utilization of EVLP [1-3]. Among programs the duration of time that is allowed between withdrawal of life support and cardiac arrest is varied with the vast majority being less than 60 minutes. Some programs have been willing to expand that time to 120 minutes. There is a modest degree of variability between centers with this risk [2].

A powerful tool that has great potential to allow for DCD lung use expansion is EVLP. As our readers know, the EVLP experience has been growing worldwide and the results that we are seeing are impressive. Combining EVLP with DCD donation has some important upsides. First, this approach allows for a period of assessment while the lung is being perfused. This is time to see if there was any injury to the lung with the hurried procurement [1,3]. Second, since there is variability in the ability to heparinize pre-recovery, the perfusion and flush period allows for washout of (micro) thrombus. Third, over time, we will have the ability to actively intervene on the lung to improve
quality. Fourth, the risk to the recipient is mitigated. With the added time to observe the donor lung on EVLP, a center can be more assured that the DCD lung is of adequate quality and then proceed to the initial steps of the operation only when they are assured that a viable transplant may be performed. This limits the risk to the recipient who may have an operation initiated and then be committed to a sub-optimal lung out of necessity.

A future and expanded potential for DCD and EVLP partnership is in the utilization of uncontrolled DCD lung donors (uDCDD). There are multiple hurdles, societal, ethical, regulatory, technical, that need to be addressed. Broad application of this uDCDD approach is in its infancy though it will be the next frontier and EVLP will need to play a role [4].

Further international experience and the sharing of protocols and techniques will undoubtedly increase the comfort with DCD lung donation. EVLP will allow for the DCD lung to be assessed thoroughly prior to transplant. This combination will increase access and improve outcomes in our lung transplant patients.

Disclosure statement: The author has no conflicts of interest to disclose.

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Angus Deaton won the 2015 Nobel memorial prize in economic science for his work on the behavior of consumption and its effect on poverty and social ills [1]. In an incisive analysis of recent data from the Centers for Disease Control, Deaton and his wife, Ann Case, concluded that the gains in life expectancy from advances in the treatment of heart disease, cancer and infectious diseases had somehow eluded a significant sector of the US population – the non-Hispanic middle aged white population (age groups of 25-45 years) [2]. As it turns out, this group is tracking a disturbing increase in death rates from drug overdose, substance abuse and suicides. Naturally, one must ask why this trend is occurring and how its unintended consequences might manifest in our world of transplantation.

There is a drug crisis in America - Whether it relates to the abuse of prescription pain killers or illicit drugs like heroin, we are in the midst of a terrifying new epidemiology where the perils of physical disease have been supplanted by mental ill health in this vulnerable population. The non-college educated non-Hispanic white middle aged man or woman in America finds isolation and exclusion from the larger economy. Poor jobs, low wages, more physically demanding jobs with prospects of injury requiring prescription pain medications, lack of healthcare security and consistent pressures of their physical environment render them vulnerable assets for transitioning into more horrendous addictive states or leading them to contemplate suicides [3].

No wonder then, that Organ Procurement Organizations are reporting a marked increase in the rates of organ donations from decedents of drug overdose, illicit substance toxic effects or suicides [4]. Naturally, this creates an unintended opportunity in organ transplantation where we are offered such organs, often with variable placement rates. Due to the “high risk” nature of such donors, care providers and their patients are reluctant to accept these organs. Furthermore, donations after cardiac death may be more common among this subset of organ donors. So, what must we, as stewards of society, do?

Even as the political establishment, government and federal as well as state legislative authorities debate the solutions to this societal illness, we can at least honor the donor and their families by giving their organs a chance to inhabit a better life. Advances in organ care, recovery and transport systems as well as enhanced algorithms for retrieving thoracic organs from deceased donors represent an important mandate for study and development [5,6]. We are in the pre-maturation cycle for embedding these opportunities into our routine practice paradigm.

This is not a curiosity but an urgent mandate. Clearly, we must redouble our efforts in avoiding loss of organs from otherwise healthy and viable donors, simply on the premise of this defined “high risk”,

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which in fact may be quite an acceptable risk in most situations. It is time that we confront this emerging epidemiology and develop solutions, together, in a scientifically rigorous but expedient manner.

So, I ask you all – What are YOU doing about it?

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References:

“Where’s the Rest of Me???”

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"It is not enough to be industrious; so are the ants. What are you industrious about?”  
-Henry David Thoreau [1]

As this author and Dr. Vincent Valentine confess and share a mutual passion regarding the movie classics, a relevant and most famous quote, "Where’s the rest of me?” contained in President Ronald Reagan’s best known film was discovered [2]. The intellectual discussion around the quality of life (QOL) of Ventricular Assist Device (VAD) patients, and their quest for finding answers to “where’s the rest of me?” has prompted providers to reassure VAD patients with a common mantra, “we are focused on providing you a life with quality.” Certainly, this should serve as a reminder of “What’s it all about?” in all endeavors for all patients in need of health care, and especially patients with failing hearts, failing lungs and recipients of replacement therapies including heart and lung transplantation. However, the focus of this brief primer is on the ever-important topic of QOL among VAD patients.

QOL is a subjective evaluation whereby an individual shares his/her overall appraisal of how happy, satisfied, and content he/she is with their life. QOL differs with every individual on the basis of each patient’s life experience, expectations, attitudes, values, and beliefs [3]. Within the VAD field we typically define QOL as an individual’s perception of the impact of the VAD on his/her life. Fortunately, numerous studies have been dedicated to evaluate this most crucial aspects of the patient’s life [4-8]. QOL can be measured with health status questionnaires that are prompted by Intermacs and/or by customized surveys designed by individual VAD programs; thus, an assurance is rendered that QOL evaluation remains threaded through-out the provider’s focus.

It is encouraging to note that QOL matters remain a significant and contemporary focus within the VAD field. The upcoming ISHLT conference agenda has allotted time to the QOL topics:

1. The Presidential Debate Topic - Destination Therapy/Heart Transplant among patients over the age of 70
2. QOL after the VAD: The impact of frailty and social behaviors on QOL
3. Engaging patients and caregivers: Successful strategies to care of patients living far away, to name a few

To those VAD patients past, present, and future, yearning to discover “Where is the rest of me,” rest assured that the providers entrusted with your care are dedicated to helping you find your answers. As Thoreau’s quote infers, those of us in the VAD profession remain focused on what it is that we are truly industrious about, the VAD patient’s QOL. That’s what it’s all about.
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References:
Use of mTOR Inhibition among Candidates on Waiting List for Lung Transplantation: Is it Time for Consensus?

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Inhibitors of the mammalian target for rapamycin (mTOR) – the two agents being sirolimus and everolimus – are commonly used as immunosuppressants in solid organ transplant. These agents are used in lung transplantation for a variety of reasons: to augment standard immunosuppression; to allow for lower levels of calcineurin inhibitors (as in the case of renal dysfunction); to protect against malignancies (especially skin malignancies); or as a means of stabilizing chronic lung allograft dysfunction (CLAD).

Two single-center trials looked at the use of sirolimus de novo at the time of transplantation (in place of azathioprine) as part of the initial immunosuppression regimen, starting at the time of transplant [1,2]. In both of these trials, an increased rate of bronchial anastomosis dehiscence was observed and patient deaths ensued. These observations resulted in a “black box warning” on drug labels for these products. Indeed, wound healing problems are recognized in heart transplant patients who take these drugs and have various types of surgical procedures [3,4].

More recently, the drug sirolimus has been shown to slow the decline in lung function in patients with the rare lung disease lymphangioleiomyomatosis (LAM) [5]. Use of the drug can stabilize these patients for extended periods of time and has impressive efficacy in controlling chylous effusion production [6] and renal angiomyolipoma and abdominal lymphangiomyoma tumor growth [7]. In other words, these drugs have become an important part of the chronic care of patients with LAM, many of whom go on to need lung transplantation if lung disease worsens.

Sirolimus has a serum half-life of about 60 hours, meaning that the drug may remain active in a patient for nearly two weeks. Everolimus has a much shorter serum half-life, at 30 hours, which still means about 7 days before the drug has been eliminated once it is stopped.

Given that the indication/need for mTOR inhibition in the setting of CLAD is not imperative and the concern around bronchial anastomosis dehiscence, and with the uncertainty in timing of the retransplant, a common practice is to stop these drugs in a patient with chronic rejection who is listed for redo lung transplant.

But given that there is a much stronger clinical imperative to use mTOR inhibition in LAM patients with severe disease, does this same approach make sense? The benefits realized by staying on the drug during a wait on the transplant list (often for many months) may outweigh the concerns around their use going into the transplant. For one thing, the tragic outcomes seen with the use of sirolimus in the two sentinel studies involved their use ongoing from the time of transplant. In the case of LAM patients awaiting transplant, they would stop the drug at the time of transplant and have diminishing
levels after the operation. Also, the use of everolimus (with the shorter terminal half-life) rather than sirolimus can offer a quicker elimination of the drug from the recipient.

In the end, it boils down to a case of weighted benefits and risk. Does the risk of not using and mTOR inhibitor in a patient with severe LAM awaiting transplant (more rapid decline in lung function, uncontrolled chylous effusions, more oxygen need, more dyspnea, a possibility of not living long enough to find a donor) outweigh a risk associated with bronchial healing problems -- in a scenario different from what was observed in the two clinical trials of concern? A study looking at everolimus use up until the time of transplant in treating idiopathic pulmonary fibrosis did not demonstrate an increased use of anastomotic dehiscence in those patients who had lung transplants during therapy [8] (albeit with a small “n”).

While some lung transplant programs are allowing for continued use of an mTOR inhibitor (often everolimus due to the quicker elimination) while awaiting transplant, many others prohibit their use. In some countries, the allocation system allows for a program to prioritize a patient for transplant in just this situation and minimize wait time “off the mTOR inhibitor”. There are not ample data to drive decision making in this situation; a risk/benefit analysis should be undertaken at each individual program in this regard. Many are calling for allowance of continued use of the drugs for LAM patients awaiting lung transplantation [9].

Disclosure statement: The author has no conflicts of interest to disclose.

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The Great Communicator: The Actor, The Gipper, The Quipster, Teflon and Alzheimer’s

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Ronald Wilson Reagan was born on February 6, 1911 in Tampico, Illinois. Son of a shoe salesman with a drinking problem and a deeply religious woman who loved the theater and encouraged him to act. His family was poor and lived as transients in different parts of Illinois before settling back in Tampico where they resided above the H.C. Pitney Variety Store before settling in Dixon, Illinois. This natural quintessential quipster would later quip that he was “living above the store again,” after moving into the White House following his election. At Dixon High School he was a mediocre student but excelled in sports, acting, and in his work as a lifeguard and served as student body president. He attended Eureka College majoring in economics and sociology and continued to excel in sports, drama and again was elected student body president. Similar to other great U.S. Presidents he worked on the student newspaper, participated in debates and enjoyed reading. But unlike other great Presidents he did not care to read history; he preferred reading adventure stories. After college, he became a sports announcer, a commentator for major league baseball and Big Ten Football then following a screen test, he earned a contract with Warner Brothers in 1937. Acting and traveling opened the door of politics for him. His film career spanned over a quarter century with appearances in over fifty films. Reagan’s most celebrated films were Knute Rockne, All American (1940) in which he played George Gipp, the famous Notre Dame football star known as “the Gipper,” and King’s Row (1942) in which he played the victim of a sadistic surgeon. The quip “Win one for the Gipper” became a rallying call and later a political slogan for Reagan at the 1988 Republican National Convention. The single line "Where’s the REST of me???” catapulted Reagan’s career when he discovered that his legs were amputated in King’s Row. Reagan would later use this line as the title of his 1965 autobiography.

He married actress Jane Wyman in 1940, enlisted in the U.S. Army in 1942 and was elected president of the Screen Actors Guild, the major labor union of the film industry. Reagan was divorced in 1949 and later married actress Nancy Davis (Anne Frances Robbins) in 1952 who would later prove to be an influential and controversial First Lady. From 1954 to 1962, Reagan was employed by General Electric and served as a host, supervisor and actor for the General Electric Theater. He delivered many public addresses on free enterprise and warned against the evils of big government, all the while he was polishing his public speaking skills. Over time, Reagan was becoming more conservative in contrast to other presidents who usually become more progressive with age. Reagan voted for Eisenhower and Nixon then abandoned the Democratic Party in 1962. He was elected governor of California from a “common sense” government campaign and served two terms from 1967 – 1975. During his tenure, California had its largest budget increase ever. After failing to win the Republican nomination for president against Nixon in 1968 and Ford in 1976, he won the nomination in 1980. **Reagan became the 40th President of the United States**, the oldest, the first actor and the only divorced person ever elected to such an office. His victory resulted in a twenty-year revival of
conservatism and made it respectable in the United States. In his 1981 inaugural address he stated, "Government is not the solution to our problem; government is the problem" in response to the apparent ineptitude and distrust of the U.S. Government, rising crime rates, drug abuse, economic woes and international problems that went on for two decades. As the oldest man elected president, his ideas were seemingly new and fresh. He was more concerned with his image rather than the details of policy or management of the government. His daily activities were carefully scripted with a uniquely disconnected style of leadership. However, early on, his presidency almost ended. On March 30, 1981 he was shot as he was leaving a Washington Hotel.

It was his quick wit and recovery that enhanced his popularity. The zingers from him on that day included: to his wife, "Honey, I forgot to duck," while intubated he wrote to a nurse, "All in all, I'd rather be in Philadelphia," and in the operating room, Reagan removed his oxygen mask and joked to all the doctors and nurses, "I hope you are all Republicans." His popularity continued to soar as he deregulated industry, reduced taxes, slowed domestic spending, returned power to the states, strengthened the military and forcefully challenged the Soviet Union for world leadership. The economy proved challenging. But Reagan’s tenacity, toughness and resiliency allowed him to deflect all criticisms and to develop a hard line in foreign policy and along with his recovery from the assassination attempt, he became known as the "Teflon President," especially when the scandals surrounding his presidency had no effect on his popularity with the public. When he was campaigning for re-election in 1984 he wanted everyone to know that "...I will not make age an issue of this campaign. I am not going to exploit for political purposes my opponent’s youth and inexperience." He won a smashing re-election victory in 1984, but late in his second term budget and trade deficits mounted, environmental problems deepened, AIDS, poverty, homelessness, drug abuse and crime soared and Reagan seemed to lack interest and ideas. The Iran-Contra affair unfolded which revealed the sale of arms to the terrorist state of Iran. Apparently these sales played a role in the release of American hostages in Lebanon with profits illegally diverted to the Contra resistance in Nicaragua. Reagan initially denied any arms-for-hostages, but later he admitted that he was wrong in this denial. Only the Teflon President could get away this. Reagan emerged from this scandal and loss of control of the Senate, unscathed. The stock market collapse of 1987 challenged “Reaganomics” – termed “voodoo economics” by George Bush Sr whereby Reagan pushed for tax cuts, reduced domestic spending, increase military spending and a balanced budget. Nevertheless, the Reagan economic boom occurred and continued through his last year as president. The focus of his last two years as president was on foreign policy. He befriended the new Soviet leader Mikhail Gorbachev who expanded democracy and civil liberties in Russia. Cuts in nuclear arsenals, agreements to eliminate intermediate-range missiles in Europe and reduction in Soviet armed forces in Eastern Europe did occur. It was June 12, 1987 when the Reagans were taken to the Reichstag building in Berlin, President Reagan was able to view the Berlin Wall from a balcony. That afternoon, he delivered his speech at the Brandenburg Gate where he asked General Secretary Gorbachev...if you seek peace, prosperity and freedom, "come here to this gate. Mr. Gorbachev, open this gate. Mr. Gorbachev, tear down this wall!" Reagan was a gifted politician who understood the American psyche, but he remained disengaged from those who surrounded him, he did not micromanage or even oversee the big picture almost to a fault. The New Deal of FDR and Great Society of LBJ remained intact with little progress on conservative social issues. However, he brought a new found respect to conservatism and his ideas on free markets became conventional
wisdom of the 1990s. All in all he restored the office of the U.S. President to a position of power and prestige. Known as the Great Communicator, Reagan fell victim to Alzheimer’s disease. He published a letter the American public of his affliction in 1994 which ended with these words, “I now begin the journey that will lead me into the sunset of my life. I know that for America there will always be a bright dawn ahead.” On the eve of the 60th anniversary of D-Day, former President Ronald Reagan died at his home in the Bel Air district of Los Angeles of pneumonia on June 5, 2004. His conditioned had greatly deteriorated as consequence of Alzheimer’s. His wife, the former first lady Nancy Reagan had announced just one month before his death how difficult it was to celebrate their 52nd anniversary when “Ronnie” had no recollection of his times with Nancy. Ronald Reagan leaves us these great words of wisdom, “Government’s view of the economy could be summed up in a few short phrases: If it moves, tax it. If it keeps moving, regulate it. And if it stops moving, subsidize it.”

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George Herbert Walker Bush was born in Milton, Massachusetts on June 12, 1924. He graduated from Phillips Academy in Andover, Massachusetts where he was secretary of the student council, president of his senior class and a member of the editorial board for the school newspaper. He joined the Navy on his 18th birthday and became the youngest naval aviator of the time during World War II. After an honorable discharge, he attended Yale University and graduated in 1948 with a BA in economics and member of Phi Beta Kappa and the secret Skull and Bones society. After moving to West Texas with his wife, Barbara Pierce Bush, and young family, he started a successful oil business in Texas. Twice elected to Congress, he became an Ambassador to the United Nations, then headed the Republican National Committee, the US Liaison Office in Peking, and the CIA. In 1980, he sought the Republican Presidential nomination but instead became Ronald Reagan’s running mate. A loyal and competent Vice-President, Bush was elected the 41st President of the United States in 1988 making him the first serving Vice President to be elected President since Martin Van Buren in 1836. He pledged to promote better education and a cleaner environment, but the firm and memorable campaign pledge that came back to haunt him stemmed from his infamous quote, “Read my lips. No new taxes.” He was forced to raise taxes. His presidency was marked by historic events in world affairs. Encouraged by glasnost and perestroika, Eastern bloc nations renounced communist rule; Germany united, and the Soviet Union disintegrated. The Cold War ended, but other wars emerged. When Iraq invaded Kuwait in 1990, Bush assembled an international coalition to reverse the aggression, culminating in the successful military operation, “Desert Storm,” which was his finest hour. But chaos and brutality reigned elsewhere in the world and almost every nation battled recession. At home, the country’s economic woes tarnished his image and, after 12 years of Republican administration and only serving one term, Americans were ready for a change.

William Jefferson Clinton was born William Jefferson Blythe III on August 19, 1946 in Hope, Arkansas, two months after his father died. He was raised in Hot Springs, Arkansas and later took his stepfather’s surname. Clinton was part of the “baby boom generation” that came of age during the Vietnam War, the civil rights and women’s liberation movement at a time when America was tuning in, turning on and dropping out. Clinton did not dropout, however we know he “never inhaled” because he said so. He did attend Georgetown University on Scholarship where he served as class president. He was elected to Phi Beta Kappa and earned a BS degree in Foreign Services. Following which he was a Rhodes Scholar to Oxford University but never received a degree. Upon returning home, he won a scholarship to Yale Law School where he met his wife, Hillary Diane Rodham of Chicago. Once situated in his home state, Clinton became a Law Professor at the University of Arkansas and was elected the youngest Governor in the country at age 32. Because of his youthful appearance, he was dubbed the “boy governor” and eventually served five terms as Governor. In 1992, Clinton joined the presidential race when the incumbent Bush looked unbeatable with very
high approval ratings as a result of the Persian Gulf War. However, Bush Sr. reneged on his campaign promise not to raise taxes and Clinton condemned Bush for this then rode an economic downturn to victory in a tight three-way race. He was elected the **42nd President of the United States in 1992**. Shortly after taking office he signed the ever popular Family and Medical Leave Act allowing unpaid leave for pregnancy or serious medical conditions. He faced early setbacks. Although he won passage of NAFTA and the “Brady Bill,” his bid for broad health care reform, led by his wife, Hillary, failed. Clinton maintained focus however on the budget deficit, crime and welfare reform. The economy boomed and he won re-election in 1996. He aimed for peace in Northern Ireland, Bosnia and the Mideast, and for racial relief at home. But he became a divisive figure himself when an on-going investigation by the Special Prosecutor’s Office revealed his illicit relationship with the White House intern, Monica Lewinsky. Clinton’s denial of the impropriety led to his 1998 impeachment by the House, though the Senate, in a partisan vote, declined to convict. Nevertheless, his success was a remarkable feat; among the key accomplishments during his Presidency included: the longest economic expansion in American history, lowest unemployment in 30 years, largest expansion of college opportunity since the GI bill, connection of 95% of schools to the Internet, lowest crime rate in 26 years, converted the largest budget deficit in American history to the largest surplus and the most diverse cabinet in American history. Finally, he raised funds for other Democrats including his wife who won a U.S Senate seat in 2000.

**George Walker Bush** was born on July 6, 1946 in New Haven, Connecticut. He was raised and attended public schools in Midland, Texas. He went to a prep school in Houston and completed high school at Phillips Academy in Massachusetts. He earned a BA degree in history from Yale University and became a member of the Skull and Bones society. George W then attended Harvard Business School and earned an MBA degree, the only U.S. President to do so. He met Laura Lane Welch in 1977 and married her later that year. As a self-admitted average student, he seemed to lack seriousness. But when he reached his mid-thirties, Bush changed and later gave up alcohol. He became more religious with more focus and became a successful businessman in the Oil industry. As a lifelong baseball fan, Bush formed a group to buy the Texas Rangers in 1989 and became the team’s managing partner. He profited over 14 million dollars from the sale of his shares in 1998. In 1994, George W became the governor of Texas on a promise to cut taxes and aid education. As a popular governor and in the wake of the 1998 Clinton impeachment scandal, party leaders encouraged Bush to run for President in 2000. He bested Senator John McCain in the Republican primaries then faced Democrat Al Gore, Clinton’s two term Vice President, in the general election. The Bush-Gore race was one of the closest and most contested in American history. When elected as the **43rd President of the United States in 2000**, he became just the second president whose father had also been president and the fourth to win the presidency while losing the popular votes. By the way George Bush’s brother Jeb was Florida’s governor at the time of the contentious and controversial election. The highlights of Presidency included his declaration of war on terrorism following 9-11 in 2001, congressional approval of widespread tax-cut bills, Medicare prescription drug coverage for seniors, enactment of the No Child Left Behind Act and allocation of billions of dollars to fight HIV/AIDS around the world. George W withdrew support of the 1997 Kyoto Protocol originally signed by Clinton to combat global warming. In his second term, his administration was criticized for it slow response to the aftermath of Hurricane Katrina. His popularity continued to sour; he took office with a federal budget surplus in 2000 which flipped to deficits following broad tax cuts,
enormous cost of fighting two wars resulting in the 2008 Great Recession, America’s worst financial crisis since the Great Depression. He has been recognized simultaneously as one of the most popular and least popular presidents in American history.

Barrack Hussein Obama was born on August 4, 1961 in Honolulu, Hawaii. His liberal minded mother, Stanley Ann Dunham from Kansas was attending the University of Hawaii when she met a Kenyan National, Barack Hussein Obama, Sr. They were married February 2, 1961 and divorced in 1964. Later she married Lolo Soetoro in 1965 and earned her degree in 1967. Little Obama and his mother moved with his step father to Jakarta, Indonesia. He was educated by his parents, the schools and culture of Indonesia until 5th grade. He relocated back to Honolulu and lived with his grandparents to attend the prestigious Punahou Academy, a private co-ed college preparatory school with a rigorous academic curriculum where he graduated in 1979. While there he wrote for the Ka Wai Ola literary journal and played for the Punahou’s State Champion basketball team. He attended Occidental College in Los Angeles for two years then transferred to Columbia University in New York where he earned a BA in political science. After working as a community organizer and on several projects on behalf of the public’s interest, he entered Harvard Law School in 1988. He became editor of the Harvard Law Review and was elected the first black president of the journal. He graduated magna cum laude in 1991 and completed his first book Dreams from My Father in 1995. He taught constitutional law at the University of Chicago Law School and joined a law firm specializing in civil rights litigation and neighborhood economic development. He was elected to the Illinois Senate in 1996 and served as a U.S. Senator from Illinois from 2005 – 2008. He announced his candidacy for President of the United States in early 2007 at the symbolic site where Lincoln gave his historic "House Divided Speech” in 1858. During Obama’s announcement of his candidacy he emphasized ending the Iraq War, reforming health care and increasing energy independence. In 2008 he defeated Senator John McCain to become the 44th President of the United States and the first African American to be elected president. Obama was re-elected in 2012. Where we are today with President Obama can be best summed up by the nationally recognized commentator and journalist Leonard Pitts from his recent editorial “If Obama wasn’t ‘black’ before, he certainly is now.”

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