April 6, 2017

DAILY Links

37th Annual Meeting & Scientific Sessions
Manchester Grand Hyatt, San Diego, CA

A Message From Your President Maryl Johnson, MD

I hope you are enjoying San Diego and the 37th Annual Meeting! What a year it's been since given the gavel to assume the role of the ISHLT president. Now I reflect on the past year to update the ISHLT members on our accomplishments. More importantly, I want to make you aware that the path being charted for the ISHLT is designed to allow ISHLT members to actively participate for future success.

Last year, the ISHLT's Strategic Framework 2016-2020 was unveiled (see May 2016 ISHLT LINKS for details). The primary focus of this year's leadership and staff is to prioritize objectives to pursue and develop tactics for implementation. The Strategic Imperatives are: Enhance Membership Value, Engage our Community Worldwide, Improve Science and Drive Innovation, and Ensure Organizational Vitality. For more information on any of these efforts, please refer to the April 2107 ISHLT Links.

A lot has been accomplished due to the efforts of our members, Councils, Committees, Board (in particular the Executive Committee), and staff, all of whom I wish to sincerely thank for their efforts and contributions. Moving the ISHLT forward is best accomplished by contributions from all of its members, so if you have been involved, I thank you. If you haven't, I encourage you to talk to your Council leadership or a society leader to indicate your specific interests.

I express sincere gratitude to Jeff Teuteberg, his program committee, and the ISHLT staff for organizing this Meeting. And, I want to thank the ISHLT for the opportunity to serve as your president over the past year. My passion for the ISHLT, its mission and the bright future that we have has only been enhanced by my more direct involvement. The society will be in excellent hands moving forward as Andy Fisher assumes the presidency this week. I pledge to Andy and to you, all ISHLT members, that I will continue to support the ISHLT in the future in whatever way I can.
I leave you with a quote that I read in a coffee house in Banff, Alberta, Canada last fall, which I think states well what is required for the ISHLT to continue to move forward.

As the ISHLT community, we have the true opportunity to improve the care of patients with advanced heart and lung disease and our likelihood of success is enhanced by working together.

> "If you want to go fast, go alone. If you want to go far, go together."
>
> -African Proverb

Small But Mighty

Preview Sunrise Symposium 5
Upcoming Opportunities and Challenges in Pediatric Lung Transplant

Wake up, wake up - it is time for pediatric lung and heart-lung to shine like the San Diego sun. Rub the sleep out of those eyes, shake off the margaritas from last night, grab a strong cup of coffee and join in the discussions around hot topics in pediatric lung and heart-lung transplant. Stuart Sweet will be discussing ECMO as a bridging strategy in newborns – who, when, why and then what. Bart Rottier will highlight the changing faces of lung/heart-lung transplant and how this is affecting which patients centers are considering and what is the optimal time for listing. Melinda Solomon will present how the ABO incompatible transplant may be one answer to address the scarcity of suitable organs in infants, as well as strategies for success. Rounding out the session will be Maria Gazzaneo discussing the pros and cons of Potts-Shunts as a possible alternative treatment to transplant in severe PH. This session has something for everyone and promises to be well worth the early morning wake up call!

Sleeping In is Overrated

Preview Sunrise Symposium 6

Even if you're a late riser, you won't need caffeine for Sunrise Symposium 6, "Those Darn CARVs," where Erika Lease, Tereza Martinu, Allan Glanville, and Christopher Ensor will keep you at the edge of your seat and tell you all you want to know about community acquired respiratory viruses in lung transplant recipients. If that wasn't enough to get you going, will take you on a trip around the world in 80 days (OK, 2 hours) at Symposium 16, where you'll learn about Zika virus, hepatitis B, tuberculosis, and travel medicine for the transplant recipient. If you love Shakespeare (or nontuberculous Mycobacteria), Symposium 23 is a must, where we'll be trying to tame the *M. abscessus* shrew. You won't want to miss Gregory Snell and Paul Corris' pro-con debate about whether patients with *M. abscessus* can be safely transplanted.

Stuck Between a Rock and a Hard Place. Or Are We?

Preview Symposium 10
Approach to the Sensitized MCS patient: Desensitization and other strategies

With a growing number of patients requiring MCS as a bridge to transplant, the immunomodulatory risk associated with MCS raises several concerns regarding transplantation of these patients. Sensitized MCS patients have a longer wait on the transplant list, putting them at a greater risk of MCS related complications and mortality. Can virtual crossmatching reduce the risks associated with transplanting sensitized MCS patients? At what calculated PRA thresholds should desensitization of MCS patients be considered? How do outcomes with desensitization after MCS compare to sensitized MCS and non-MCS transplant recipients. Are the risks worth the benefit? Don't miss this stimulating session in Symposium 10 as presenter Jignesh Patel MD, PhD offers insight to these questions and more!

Pursuit of Perfection

Preview Sunrise Symposium 11
There is No Such Thing as Perfect: Selecting Recipients for Lung Transplantation

Lung transplant recipient selection is often a challenging task and may vary immensely between institutions. This symposium chaired by Rupal Shah, MD and Daniel C. Chambers, MBBS, MRCP, FRACP, MD, MD will focus on physiologic, psychosocial, and controversial transplant recipient selection criteria. The session will begin with Dr. Jonathan Singer discussing how older and sicker patients are often prioritized to receive lung transplantation due to advances in medical therapy and organ allocation. He will focus on ways to improve risk stratification of lung transplant candidates by reviewing newer metrics for evaluating age, body composition, and physiologic frailty. Next Dr. James Blumenthal will review approaches to key bio-psycho-social factors in lung transplant candidate selection and will evaluate these factors as related to outcomes following lung transplantation. Finally, Dr. Jens Gottlieb will discuss how candidate selection may vary between institutions and will examine 'extended criteria' in candidates who may fall outside the limits of age, BMI, presence of comorbidities and mechanical support. Don't miss this controversial and stimulating discussion on lung transplant candidate selection!

President's Cocktail Reception Tonight
The reception will be held tonight 8:00-9:30 PM at the USS Midway Museum, the longest serving US Navy aircraft carrier of the 20th century. Located at 910 N. Harbor Dr. Tickets are required.

ID Under the Bright Lights

Enter stage left into a crowded room with bright Hollywood lighting (or at least that's how it felt sitting at the moderator's table). It's not every day that transplant ID has a Hollywood moment, but I love it when it happens.

This morning opened with a hugely successful joint, ISHLT/ESCMID symposium (SYMP-07) that is, entitled "Ongoing Challenges in Transplant Infectious Diseases." Barbara Alexander mapped the progress made in non-cultural methods for diagnosis and prevention of invasive fungal infections since 2006 and highlighted more recent improvements in the field. We're certainly "not there yet," but we have a roadmap. The same can be said for inhaled antimicrobials, infections in thoracic organ transplant recipients on ECMO, hepatitis C in donors and thoracic transplant recipients, HIV infection in thoracic organ transplantation and MCS, and the role of EBV and anellovirus viremia in predicting infection risk. Sometimes being left with more questions than answers is a good thing, and there was palpable excitement about tackling the unknowns at the ID Council Scientific Meeting. Can we ask the right questions?

It was a full house, as we moved from challenges to "Cutting Edge Updates in Infectious Diseases (ORAL 07)." Colleagues from the University of Toronto discussed risk factors for invasive aspergillosis in lung transplant recipients, as well as use of the Aspergillus galactomannan in exhaled breath condensate for the diagnosis of invasive aspergillosis in lung transplant recipients. Jutta Preiksaitis then discussed the University of Alberta's experience with CMV and its prevention strategies in heart and lung transplant. We also learned more about invasive *Mycobacterium abscessus* infections in heart transplant recipients at Duke from Eileen Maziarz (a great prequel to Symposium 23, "The Taming of the Shrew" at 4pm tomorrow – don't miss it!!), as well as clinical and microbiologic characteristics of infections in LVAD recipients from Mary Bradbury at Inova Fairfax Hospital. The session concluded with Haifa Lyster from Royal Brompton & Harefiled NHS Foundation presenting exciting results from an *ex- vivo* experiment showing sequestration of posaconazole by the ECMO circuit.

Today's presentations deserved a standing ovation. And we've only just begun...

Moving Boundaries: Pumps Next Steps

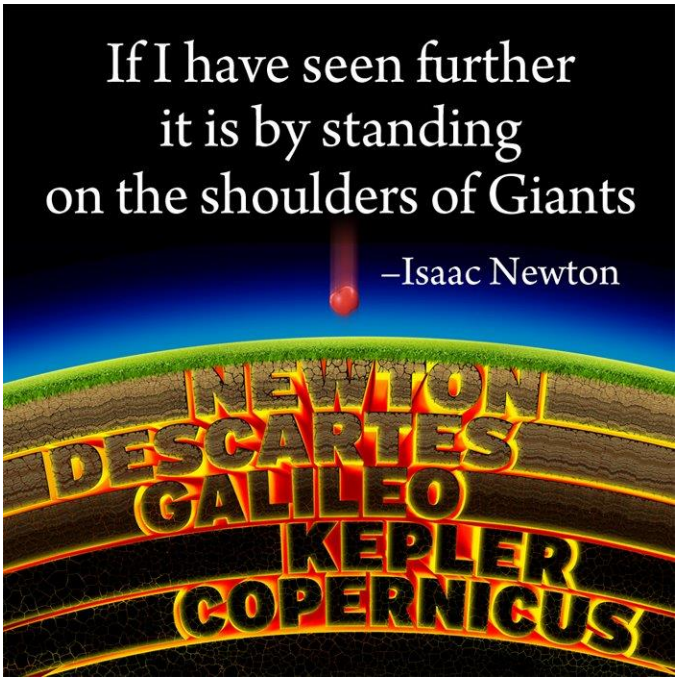
Review of Wednesday's Opening Plenary Featured Abstracts

The first featured abstract was given by Dr. Milano representing the ENDURANCE trial principal investigators. Two years ago the results of the original ENDURANCE destination therapy trial were presented at the ISHLT annual meeting in Nice showing non-inferiority of the HVAD device for primary endpoint in destination therapy patients compared to the HeartMate II device. However, a higher rate of hemorrhagic strokes were seen, especially for patients with high blood pressure. Yesterday, the results of the ENDURANCE Supplement Trial were presented, a trial that used the same protocol as for the original ENDURANCE but enrolled additional patients to give a more detailed analysis on the performance of the HVAD device. In summary, the HVAD device still had a slightly higher but not significant rate of stroke. The HVAD proved to be superior with regards to death, disabling stroke, device or urgent transplant at 12 months. The incidence of pump exchange was lower. Patients with both devices had a comparable quality of life after one year. This presentation was discussed by Vivek Rao, MD, PhD. What were the reasons for the improvement to the previous trial? A smaller coring device and new sintering of the inflow cannula may be responsible together with a better blood pressure control.

The second featured abstract, presented by Dr. Goldstein representing the study principal investigators, gave a detailed view on the results from the MOMENTUM 3 pivotal trial. This study is a prospective, multi-center, unblinded randomized study comparing the HeartMate 3 device to the HeartMate II device. The first six months after implantation were evaluated for factors associated with outcomes to identify patients who may benefit most from the HM 3 implantation compared to the HM II device. Gender, therapeutic intent, severity of illness and race, when adjusted for age, did not influence the primary outcome success. These results were discussed by Jan D. Schmitto, MD, PhD, who implanted the first HeartMate 3 device and is one of the most experienced surgeons with the HM 3 device. Which is the best device for the individual patient? What is the role of the HM 3 device after the improved data with HM 3 device?

Standing Ovation For a Giant

Review of Pioneer Lecture



To become a Giant he stood on the shoulders of Giants. Dr Stuart Jamieson received a standing ovation after his ISHLT pioneer award lecture during the opening plenary session. His lecture nicely underscored why the impressive contributions in the field of cardiothoracic surgery and transplantation made him a Giant. Trained and mentored by other Giants like Lewis, Lillehei and Shumway, Jamieson pioneered and moved the boundaries of cardiothoracic surgery and transplantation in the last decades.

Besides being an extraordinary surgeon, he was visionary in doing research giving the fact that his laboratory and animal experiments resulted in the clinical utility of the heart-lung machine, cold preservation of donor lungs with hypothermic crystalloid, and the use of cyclosporine as first immunosuppressive drugs used in the monkey 'Mom'. His surgical techniques regarding bilateral lung transplantations, thromboembolic endarterectomies, and surgical instruments are still used in programs around the world.

The longest living heart and lung transplant patients like many others trusted their lives in his hands. Jamieson said about the first open heart surgery 'Lewis brought the can opener to the picnic', we might say that Jamieson turned the picnic into a culinary dinner.

The Good, Bad and Ugly of Transplant! Should Patients be Declined for Transplant Due to Non-adherence?

Review Symposium 2
When Should We Call It Quits? Intervention Strategies and Outcomes for Medical Non-Adherence

Clinical trials on non-adherence are lacking causing gaps and challenges on arguably the most important factors for the success of post MCS/transplant patient outcomes. There is a panoply of interventions for adherence: Face-to-face, electronic, behavior modification etc. Interventions are so varied that the best mode of therapy remains elusive. Education alone is not enough. According to Dr. Mary Amanda Dew, University of Pittsburgh School of Medicine, "The one size fits all approach does not work." It's unclear if clinical outcomes have improved with such interventions. 12 trials in the last 18 years, were limited by a short study periods and no clinical outcomes making these very difficult to validate. There was a randomized trial with a personal smartphone application, "Pocket Path". The app was customized to the specific patient's needs. This sample size was 201 and only looked at the use of the app for 1 year. This trial dissolved over time. MAESTRO-TX Study included patients who were > 1 year post transplant and was tailored based on patient needs. The impact of this study included dosing and timing adherence but was difficult to assess. Next steps would be a measurable program that is adaptable in routine practice. With the success of the mobile apps, possible consideration to a more fine-tuned mobile monitoring smartphone application. The caveat is the advanced aging population is not tech savvy. Let's conclude by saying we need more work in this area toward the trends of MCS/transplant medical adherence.

Piecing Together the Puzzle of Predicting PGD

Review Symposium 3
Review of Risk Factors for PGD: Donor, Recipient, and Surgical Procedure

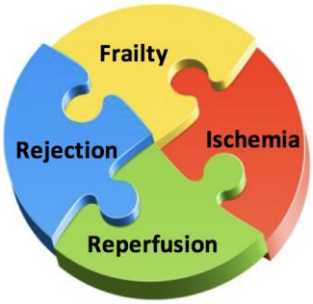
Dr. Jennifer Cook began her session with a few questions for the audience that clearly set the stage for the relevance of the coming discussion. "How many of you have had a heart transplant patient develop Primary Graft Dysfunction?" By a show of hands, it was obvious that nearly every person in this packed session had experience with this unfortunate scenario. "Now lower your hand if you were able to predict at the time of transplant that the patient would have developed PGD." The room was still.

So how can we do a better job of predicting PGD?
Dr. Cook begins her presentation by reviewing the RADIAL score, the only validated scoring system for PGD. This tool was developed based on a multivariate analysis from a single-system transplant center with 621 transplant patients from 1984-2006. (*Segovia J et al JHLT 2011;30:644*) In this study, the incidence of PGD was 9%, while mortality was 80%. So how useful is this tool today when we know that rates of PGD have nearly tripled from the early 2000s to 2013? A more contemporary analysis of the RADIAL score took place in

R = RA pressure ≥ 10 mm Hg
A = Age (recipient) ≥ 60 years
D = Diabetes mellitus
I = Inotrope dependence
A = Age (donor) ≥ 30 years
L = Length of ischemic time ≥ 240 min

14 transplant centers (n=698) from 2006-2010 and found an incidence of PGD of 22% with a 30 day mortality of 40% and an in-hospital mortality of 58%. (*Cosio Carmena MD et al JHLT 2013;32:1187-95*) This study found that patients who developed PGD had a RADIAL score of 2.78 compared to 2.48 for patients without PGD. While this finding was statistically significant, a difference of 2.78 and 2.48 is hardly a clinically meaningful difference as Dr. Cook points out. However, the authors of this study did risk stratify patients based on RADIAL scores: low risk (0-1 points), intermediate risk (2 points), and high risk (3-6 points) which correlated with PGD incidence of 12.1%, 19.4%, and 27.5% respectively. (High risk patients OR=2.76). Again Dr. Cook points out several limitations of this study including the relative low number of MCS patients as BTT (~8%) and the combined definition of PGD without distinguishing between right, left, and bi-ventricular failure which has since been defined in the 2014 ISHLT Consensus Statement. Finally, Dr. Cook reviewed the most recent analysis of risk factors in PGD as defined by the ISHLT consensus classifications. This study identified three donor related variables (female, BMI mismatch >20%, & ischemic time >240 min) and four recipient related variables (female, congenital heart disease, pre-transplant HGb <10g/dL, & pre-transplant PVR >3WU) as being independently associated with increased odds for developing severe PGD. (*Sabatino M et al JHLT 2017; ePub*) High risk of developing severe PGD was defined as having 1 donor related risk factor and 2 recipient related risk factors. The authors of this study also calculated RADIAL scores and found that a RADIAL score >2 was associated with in-hospital death in patients with PGD.

To summarize Dr. Cook points out that we have several useful data points to help predict patients that may develop PGD but it's still not enough. Possibly our future aim should be at better understanding the underlying mechanism of PGD? She suggests we start by looking more closely at a few key pieces that may be important pieces of the puzzle: frailty, rejection, reperfusion, ischemia.



Too Little, Too Late

Review Symposium 3
Primary Graft Dysfunction (PGD) and Vasoplegia After Heart Transplantation: Sink or Swim

Wednesday started with a session about primary graft dysfunction, one of the most feared complications after orthotropic heart transplantation associated with a high mortality chaired by Scott Silvestry, MD, and Hermann Reichenspurner, MD, PhD. At first, Jon A. Kobashigawa, MD reviewed existing and updated the knowledge on primary graft dysfunction (PGD) and vasoplegia after heart transplantation in light of the ISHLT 2014 defined PGD criteria. Jennifer Cook, MD, gave the next presentation focused on existing avoidable and not-avoidable risk factors for PGD and Hiroo Takayama, MD, highlighted that unfortunately, in some cases, despite the lack of risk factors, no cause for the PGD could have been identified and reported by the Columbia experience on how to treat PGD. Maria M Patarroyo Aponte, MD and Paul J Mohacsi, MD try to adopt knowledge gained in surgery for mechanical circulatory support and non-transplant surgery for heart transplantation. All speakers and panelists agreed that the best is to avoid this scenario. Interestingly, Andre R Simon, MD, PhD presented the UK

prospective PGD study on donor, recipient, and surgical risk factors. He emphasized the role of the ex-vivo perfusion during organ retrieval and the possible benefits in terms of avoidance of a PGD. The session ended with a panel discussion with the conclusion that the best treatment of PGD is avoidance and the treatment is unfortunately too little and too late. Once, PGD occurs immediate intervention is imperative to reduce mortalit

Plenary Session Live Stream Event
Join us live for our 3 plenary sessions this week for stimulating conversations and lively debate.
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LAS – What's in a Score?

Review Oral Session 4
Donor Lung Allocation Strategies

Alexander Aretakis discussed how the rate of change in LAS (lung allocation score) correlates to clinical outcomes. While patients whose LAS increases rapidly have predictable worse waitlist outcomes, rapidly increasing LAS decreases time to transplant for COPD and CF, but not for Pulmonary Fibrosis. Brian Lim discussed how the LAS has narrowed racial and ethnic disparities in adult lung transplant outcomes. Alexander Bernhardt shared his center's comparative study using the ISHLT database to look at old for old transplants as a way to potentially expand the donor pool. Wiebke Sommer discussed their success in transplanting lungs from primarily young donors with PAE as an initial cause of death. The Louisville group shared two abstracts. The first discussed how their center generated a scoring system based on donor characteristics to identify donor risk profiles pre transplant. Given the increasing opioid epidemic in the US, they also shared timely and relevant data indicating post lung transplant survival is equivalent between appropriately selected drug and non-drug intoxicated donors.

All Rules Change in the Immune Suppressed

Review ISHLT Academy
Core Competencies in Infectious Diseases in Thoracic Transplantation and Mechanical Circulatory Support

In cardiothoracic transplantation managing infections is a great deal in daily clinical practice. The Academy meeting on Tuesday aimed to update the transplant clinician about the evaluation of potential cardiothoracic transplant recipients and donors, and identify bacterial, fungal, viral and parasitic infectious diseases.

'Expect the unexpected', this not only accounts for managing active infections in cardiothoracic transplant patients, but also for referred potential recipients.
'What about HIV?' Due to the potential pro-atherogenic effect in HIV, comorbidity such as hypertension and diabetes the landscape for the HIV patient in relation to cardiac transplantation changed. Those with stable disease, no active opportunistic infection or malignancies, in the absence of coinfections like HCV, HBV, might be considered for

transplantation. There is no data available *yet* in lung transplantation. Considering HIV patients for cardiothoracic transplantation illustrates that transplant medicine is moving the boundaries. The future in cardiothoracic transplantation in relation to infectious disease might be that '*All rules evolve in the immune suppressed'.*

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4) Express yourself! Excited about a certain symposium? Tell us which one!

We will be Tweeting during the Annual Meeting using the hashtag **#ISHLT2017**.

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