April 12, 2018

DAILY Links

38th Annual Meeting & Scientific Sessions
The Acropolis, Nice, France

A Message from Your President Andy Fisher, MD

Bonjour! I hope you are enjoying the 38th Annual Meeting. A year has passed quickly since I took on the role of ISHLT President. As I look back on the past year on our accomplishments, I am pleased to report that the Society remains in good health and continues to grow.

Our membership numbers continue to increase as does overall attendance at our annual meeting and this year we hit a record high for abstract submissions. This all goes to support the fact we strive to offer a value proposition to our members from all over the world.

It was a pleasure to formally announce that our 2021 Annual Meeting will be hosted in Sydney Australia - the first time, in more than 20 years, our meeting will be held in the Asia-Pacific.

The accomplishments of the Society are only possible due to the efforts of our members, Councils, Committees, the Board of Directors, Executive Committee, and importantly, the ISHLT staff. To all, I say thank you for your efforts and contributions. I would especially like to thank Christian Benden, his program committee, and the ISHLT staff for organizing this amazing meeting in Nice.

As Jeffrey Teuteberg assumes the presidency this week, I wish him well and know that ISHLT is in good hands for the year ahead.

Working together, through research and collaboration, we have the opportunity to influence and improve the care of patients with advanced heart and lung disease. Thank you for the opportunity to serve the ISHLT community.

OPENING PLENARY

Lifetime Achievement Award

The Lifetime Achievement Award was presented during the Opening Plenary to O. Howard (Bud) Frazier, MD, Texas Heart Institute in Houston, TX.

Finally! 4evergreen, 4evermore, 4everlung. *A Star is Born*!

Jens Gottlieb presented results of this multicenter collaborative trial in the opening plenary. Patients 3-18 months post transplant were randomized 1:1 to open label quadruple agent immunosuppression with reduced target CNI level (tacrolimus 3-5) everolimus (3-5) in addition to cell cycle inhibitor and prednisolone. A total of 130 patients were randomized. At 12 months there was a difference in GFR of 10ml/min in favor of the quadruple regimen. Patients with the most inferior GFR at baseline (40-60ml/min) stood to gain the most as 30% of patients had improved renal function over the study duration. Acute rejection episodes did not vary between the groups. There was a nonsignificant trend toward more CLAD within the triple therapy group and no difference in group. Time will tell whether the intervention might improve disappointingly high rates of end stage renal disease associated with our specialty.

Review Symposium 7: Cutting Edge CTEPH

Leave No Clot Behind

Can we predict which patients have the best outcomes after pulmonary endarterectomy? And how do we do an endarterectomy for that matter? The distinct themes for the first scientific session of Nice 2018.

"A wise doctor does not mutter incantations over a sore that needs the knife"
- Sophocles 406 BC

UCSD 'kicked off' the meeting demonstrating that RV-PA coupling, pulmonary arterial compliance and elastance can complement standard hemodynamics in predicting length of stay and suboptimal postoperative hemodynamic response. The Cleveland group discussed metabolomics demonstrating increased levels of fatty acids in CTEPH patient compared to IPAH patients and health controls- is clot burden or pulmonary hypertension responsible? The Baltimore group used a surgical thrombectomy series performed for acute PE to develop a scoring system to identify patients with chronic thromboembolic disease. Symptom duration (>4 weeks), pulmonary artery size (>3.5cm) and RV hypertrophy were all predictive of chronic disease requiring formal endarterectomy.

UCSD continued to push the CTEPH surgical boundaries sharing their experience of minimally invasive (or access) endarterectomy. Performed through mini thoracotomies, the results of their first 5 cases in selected patients were impressive and comparable to the conventional technique. Continuing the technical theme, Pavia shared their modified circulatory arrest protocol allowing longer total circulatory arrest time. It was suggested that this allowed superior clearance as demonstrated by number of reopened branches- this unsurprisingly correlated strongly with hemodynamic improvement parameters. Finally, the Bangalorian experience and case series provoked interesting discussion about ECLS strategies in salvaging the failing postoperative patient.

*"Three things cannot be long hidden: the sun, the moon and the **truth**."*

-Buddha

100 Years Later, We're Still Searching for the Truth
The 1918 Flu Pandemic

An important and almost incomprehensible fact about the Spanish flu is that it killed millions of people in a year or less. Nothing else: no infection, no war, no famine – has ever killed so many in such a short period. And yet it has never inspired awe, not in 1918 or 100 years later.

Epidemic diseases have often changed the course of human history – the death of a world leader, an epidemic before a great battle – but few diseases have accomplished it through sheer brute force. The deadliest epidemic of all time not smallpox, not the Black Death – it was the 1918 flu. In one year, an estimated 50 to 100 million people died, and that's out of a global population of 1.8 billion. In America alone, 675,000 died of the flu.

More Americans died of the flu in a single year than in WWI, WWII, Korea and Vietnam combined. It was one of the great watershed events in the history of the world, and yet it remains shrouded in a cloud.

One-hundred years ago in a simpler era – before television, computers, smart phones and the internet, it was the summer of 1918. The US was enjoying warm weather and general prosperity. For most, their biggest worry was the war in Europe, WWI, the war to end all wars. The flu had passed through the spring of 1918 bringing mild fever and aches, but nothing unusual.

Nobody knows precisely where the 1918 flu began, but evidence points to Haskell County, Kansas. And it may have stayed within Kansas, except for one unalterable fact: We were at war. Flu victims can spread the disease for up to a week. In an isolated place like Haskell County, the flu might have quickly died out after being passed back and forth among the local population. But in war time, people are moving between populations more often, and in greater numbers. The timing of the epidemic could not have been worse.

Why had this mild strain of flu suddenly become so virulent? Several hypotheses were proposed: A new and entirely different strain had emerged, or perhaps a genetic mutation had altered the original strain, or maybe two different viruses had fused together to create a new strain.

Viruses are mysterious. They generally consist of a core of RNA or DNA surrounded by a membrane or capsule. RNA is a single strand of genes; DNA is two complementary strands joined together in that classic double helix. Unlike cells, viruses cannot replicate by themselves: They need to take over the protein synthesis factory in a living cell and reprogram it to make copies of the virus.

Influenza is an RNA virus with eight separate genes enclosed in a membrane with spikes. The virus is very small, about 1/10,000 of a millimeter. Viruses are so small that an area the size of the head of a pin could hold a billion of them.

No one was prepared to deal with the thousands of sick and dying men, confined in the living hell that confined military conditions provided. The flu soon spread to French and British troops, and allied soldiers took it home to civilians when they went on leave. The virus spread rapidly through soldiers, POW's and civilians spreading to Germany, Russia, China, India, Southeast Asia and down into Spain, becoming the true global pandemic. It was dubbed the "Spanish Flu" but only because the press started to take notice at the time it happened to be hitting Spain.

> *"The worst pandemic in modern history was the Spanish flu of 1918, which killed tens of millions of people. Today, with how interconnected the world is, it would spread faster."*
>
> *- Bill Gates*

Review Symposium 1: Drug Therapies for Pulmonary Hypertension are Needed to Target the Right Ventricle

If Truth be Told, We Need More Drugs…

In Wednesday's Symposium 1: The Devil Wears Prada – The Role of the RV in Advanced Heart failure and LVADs, Marc Simon, MD from the University of Pittsburgh reviewed available literature for treating pulmonary hypertension in patients with advanced heart failure. Dr. Simon began his presentation echoing the sentiments of several previous presenters: RV failure is associated with mortality. Current available PH therapies such as prostacyclin analogs, endothelin receptor blockers (ERA), phosphodiesterase type 5 (PDE5) inhibitors and soluble guanylyl cyclase (sGC) inducers have several proposed cardiac effects including increased angiogenesis, decreased fibrosis, deceased cardiomyocyte apoptosis, and increased contractility that should have a positive impact on the RV. While these agents have all been shown to improve cardiac output in PAH clinical trials, the findings have not been as positive in heart failure patients with reduced ejection fraction (HFrEF). Specifically, prostacyclin analogs & ERAs have been associated with worse outcomes in this patient population while PDE5 inhibitors have had mixed results. Studies are ongoing to determine if any of these agents may have a benefit in patients with heart failure and preserved ejection fraction (HFpEF) or MCS.

If traditional PH therapies are ineffective, what other options do we have? Dr. Simon reviewed data supporting the use of low dose carvedilol which may reduce fibrosis, proliferation, apoptosis, pro-inflammatory factors and ultimately RV metabolism. Agents that affect the renin-angiotensin system have for the most part shown mixed results, apart from aldosterone blockers when used in combination with ambrisentan. This combination has retrospectively been associated with improved 6-minute walk distance tests and functional class, however prospective trials are ongoing.

Ultimately, patients with pulmonary hypertension and heart failure have limited options for targeting RV dysfunction. Newer mechanisms for targeting RV dysfunction (RV metabolism, fibrosis, hypertrophy, and oxidative stress) are being researched. Importantly, Dr. Simon emphasized that maybe our first step is to identify the right outcome to study. Our pursuit for answers continues as the purse contains the details.

Review Oral Session 12: The Leading Edge: Novel Practices in Patient Care Pathways

The Future is Now the Present

Following the exciting launch of a new ISHLT website in Wednesday morning's presidential address, powering us into the modern technology era, this oral NHSAH session

highlighted how we are engaging with our patients with novel technology practices such as Telehealth. Anne Luke from Montefiore Medical Center in New York, USA gave us results from her trial looking at the introduction of an app to monitor patient well-being this was followed by Mohammad Alrawashdeh from Pittsburgh, who gave us his PhD results on how interactive health technologies are impacting the clinicians and their perceptions of how their workflows have changed since adopting technology.

The theme of reducing hospital readmissions ran throughout the session, no more so in the discussions from Felicia Schenkel, USA and Aman Sidhu from Canada. Last but certainly not least, we were privileged in welcoming one the pioneers in interactive technology, Annette DeVito Dabbs from Pittsburgh, who gave us valuable tips in how to create and work with technology, as we boldly enter a new frontier in healthcare medicine.

Review Mini Oral 5: Pediatric Thoracic Transplantation
Youth Finding the Truth

The search for truth and understanding was on rapid fire in this session. The first discussion reviewed the new pediatric heart allocation system and how there was a doubling of those children listed 1A and a tripling of exceptions to be listed 1A. The only lung transplant discussion was next and showed that children listed for retransplantation had the lowest waitlist survival when listed at an adult center and unfortunately, the majority of retransplant candidates are listed at adult centers. Data from the Pediatric Heart Transplant Society was presented and concluded that children with a diagnosis of heterotaxy had worse survival post transplant compared to those with congenital heart disease and cardiomyopathy. A review from UNOS showed that pediatric heart donors with reduced EF (<55%) and a longer time (>5 days) from declaration of brain death to aortic cross clamp time was associated with worse recipient survival. In the ongoing search, mycophenolate mofetil was discussed and it was concluded that trough monitoring underestimates actual drug exposure and many patients may be actual getting higher doses than needed. Next, drug levels of CNIs were examined and it was found that rates of cardiac rejection were increased when these levels were sub therapeutic. Associated with this finding, investigators in Seattle showed that patients who were poorly compliant with their outpatient follow up appointments had an increased risk for mortality.

The next presenter showed a lot of guts, and concluded that reduced biodiversity of the microbiome was associated with an increased risk of post transplant diarrhea. In another study using PHTS data combined with the Pedimacs registry data showed that patients with an infection while on a VAD did not have an increased risk of infection or rejection post transplant. Next, a single center study concluded that children with heart failure and malnutrition had improved nutritional rehabilitation while on a VAD compared to those being medically managed. A UK experience was then outlined regarding their use of the HeartMate VAD. This proved to be a positive experience with a good quality of life and functional status for these patients. Finally, virtual reality was used to allow a surgeon to fit a total artificial heart in 10 virtual patients. Far out.

Whew, what a ride. Progress was made, some truths were found but the search will continue...

COMING ATTRACTIONS

Preview Symposium 17: Rapid Update on MCS Complications and Management: The Unpublished

Quests to Questions

If you work in the world of MCS, you've probably read countless articles on management and complications of LVADs. You may have attended session after session to learn from the best and brightest in the field with hopes to find answers to your questions. Do you ever feel as if your search for answers ends only with new questions? If so, you won't want to miss this comprehensive update on unpublished data in MCS management.

To kick off the session, Andre Vincentelli, MD, PhD will be discussing new developments in what tends to be a necessary evil of MCS management: anticoagulation strategies. Next, Omar Saeed, MD will shed light on a question that comes up frequently: when is hemolysis clinically relevant? Joshua Willey, MD, MAS be discussing one of the most feared complications in LVAD patients: stroke and how to manage it. Next, Jennifer Cowger, MD, MS will describe how to assess aortic insufficiency in patients with LVADs, its clinical relevance, and considerations for management. Saima Aslam, MD, MS will expose more information on the pesky issue of chronic infections in destination therapy LVADs. Susan Joseph, MD will review invasive vs. noninvasive device optimization. Nir Uriel, MD will follow with a discussion of pulmonary artery sensors. Finally, Evgenij Potapov, MD, PhD will discuss ancillary procedures during LVAD placement relative to the prevention of long term complications. Don't miss this informative session that promises to aid in your never-ending search for answers and hopefully contribute to the success of your patients!

Preview Symposium 22: CMV in thoracic organ transplant
CMV – The Truth is Out There

Different transplant centers – different approaches to CMV. Experiencing different programs may leave you uncertain and searching for answers. This symposium may help! How much CMV do you need before it's a problem? When do the toxicities of prophylaxis and treatment outweigh the potential advantages? How long should we continue prophylaxis? Can we better define who to target our prophylaxis for? What if ganciclovir doesn't work and what's new on the horizon? There are many unanswered questions that may be cleared up after tomorrow's session.

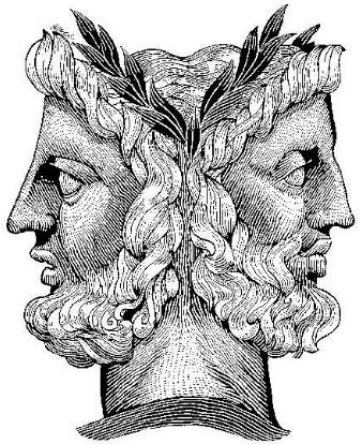
Preview Symposium 23 – Too Little or Too Much: Controversies in Monitoring After Pediatric Thoracic Transplantation

A Fork in the Fork in the Road: Is There a Best Path or Should We Just Take It?

> *When You Come to a **Fork in the Road**, Take It.*
>
> *- Yogi Berra*

We all love a good controversy and this one will be sure to create a productive conversation of varying opinions on how best to monitor patients after thoracic transplantation. This session will start with a discussion on emerging biomarkers after transplantation, which is an exciting field with great research underway. There will then be two separate debates, the first being the use of bronchoscopy after lung transplant and then use of cardiac catheterization after heart transplant. Each provider will have 15 minutes to make their case for or against their monitoring modality with an additional 5 minutes for rebuttal. This will be sure to spark a lively discussion and if you take care of this patient population, this is a must-see debate.

Contranyms: Two Sides to the Truth



Cleave (verb)

1. To split or divide by cutting
2. To stick closely to; to cling to

The word *cleave* has two meanings that are the exact opposite of each other: to split apart and to stick closely to. Words with two meanings that are the exact opposite of each other, their own antonyms, are called *contranyms*, or *Janus words*, named after the Roman god Janus, who is the two-faced god of gates, doorways, and beginning and endings.

Buckle is another Janus word, meaning either "to fasten together," as in "I buckled my belt," or to "bend and break," as in "My knees buckled."

In the same way, *bolt* can mean either "to secure and lock," as in "Bolt the door," or "to run; to make a sudden, swift dash," as in "The rabbit bolted toward the undergrowth when it saw the dog."

The first meaning of *cleave*, "to split or divide by cutting," appears in this context sentence: "If you want to cleave the roast, use the sharp meat cleaver."

The second definition of *cleave*, "to cling to; adhere closely to; stick to," appears in this sentence, "Despite the temptations of college life, he cleaved to the principles his parents had instilled in him in his youth." The reason *cleave* has two opposite meanings is that it really is two distinct words that happen to be spelled in the same way. These two meanings evolved from two different words of Germanic origin.

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