33rd Annual Meeting and Scientific Sessions

DAILY Links

April 16 -21, 2012 • Prague, Czech Republic

Contributing Writers:
Alexander Bernhardt MD and Shiwan Shah DO
Newsletter Contact:
Lisa deLeon
972.467.9602

Schedule at a Glance

7:00am – 7:00pm
Registration Desk Open

8:00am – 9:15am
Concurrent Symposium 1:
A Lifecycle Journey in Advanced Heart Failure and Transplantation
(Meeting Hall 4)

Concurrent Session 7:
The Dark Side of VADs
(Congress Hall)

Concurrent Session 8:
Heart Transplantation: Trends in Complications and Risk Factors
(Forum Hall)

Concurrent Session 9:
Lessons from Lung Transplant Database Analysis
(Meeting Hall 1)

Concurrent Session 10:
Pulmonary Hypertension: Advances in Diagnosis and Therapy
(Panorama Hall)

Concurrent Session 11:
Tolerance: To the Bench and Back
(Meeting Hall 5)

Concurrent Session 12:
Bad Bugs: Donors, Recipients and the

PREVIEW: Extra, Extra, Read All About It – Advances in Pulmonary Hypertension

Pulmonary hypertension, either primary or secondary to heart or lung diseases is a severe condition which should be diagnosed and treated early and effectively. Today's **Concurrent Abstract Session 10: PH: Advances in Diagnosis and Therapy** addresses these issues and is chaired by Dr. Evelyn Horn and Dr. George Javorsky. The first presentation delivered by Dr. R.C. Deano will present data from a multi-center study on the referral of pulmonary hypertension (PH) patients. They find patients referred to PH centers for diagnosis and treatment are often misdiagnosed, resulting in failure to follow the recommended diagnostic algorithm, particularly right heart catheterization.

The subsequent presentations deal with innovative pharmaceutical treatments of PH. Epoprostenol AM (Veletri®2) is a novel formulation of epoprostenol sodium that has increased room temperature stability. Early results of a multi-center trial will be presented. Next, Dr. S. Shapiro will give data on the long-term addition of ambrisentan therapy to PAH patients with a sub-optimal response to PDE5i therapy after 48 weeks. Also, early results of an open label non-randomized pilot study to evaluate the safety of a novel NO delivery system in patients being evaluated for heart transplantation will be provided.

Dr. K.S. Motonaga from the Stanford group evaluates the role of cardiac resynchronization therapy in PH pediatric patients. They found that pediatric patients with PH have abnormal mechanical and electrical activation of the Right Ventricle (RV) whencompared to normal subjects. They concluded that dyssynchrony might play a role in RV dysfunction seen in PH. The session ends with a presentation by Dr. K.M. Swetz from the Mayo clinic on "Patient and Clinician Perceptions of Palliative Care in Pulmonary Arterial Hypertension" in which palliative care and quality of life will be discussed.

Skepticism

Will the ISHLT 2012 Prague initiate a Renaissance in Heart and Lung Transplantation with the replacement of mechanical devices? Only time will tell as nearly as 500 years have proven the amazing feats of 1543 when Nicolaus Copernicus published Orbium Celestium and when Andreas Vesalius of Brussels published the most accurate and comprehensive anatomical text at the time. Not only did Vesalius meticulously dissect and systemically describe the human body, but more importantly he taught us not to believe all we see, hear and read unless it is verified. After debunking 1500 years of Galenic medicine, he left us with this most important tool, skepticism.

PREVIEW: Every Journey Begins with a Single Step …Unless You Have Advanced Heart Failure

This year's topic in the series entitled "A Lifecycle Journey in…," sponsored by the ISHLT Pharmacy and Pharmacology Council, is "**A Lifecycle Journey in Advanced Heart Failure and Transplantation"**. This Thursday morning symposium chaired by Dr. Patricia A. Uber and Dr. Andreas Zuckermann, focuses on the therapeutic aspects involving emerging or established knowledge in the pharmacological and pharmacy aspects of disease. In Thursday's session, the focus will be the lifecycle of advanced heart failure and cardiac transplantation with special emphasis on the "journey points" of Mechanical Circulatory Support (MCS), anticoagulation, post-transplant development of Antibody Mediated

Consequences
(North Hall)

9:45 am – 11:30
Plenary Session
ISHLT Traditions
(Congress Hall)

Noon – 1:15pm
Concurrent Symposium 2:
Focus on Caregivers: Investing in Our Patients' Future
(Meeting Hall 5)

Concurrent Session 13:
MCS: Balancing on the Razor's Edge
(Congress Hall)

Concurrent Session 14:
What's New in Immune Surveillance in Heart Transplantation
(Forum Hall)

Concurrent Session 15:
Clinical Aspects of Lung Transplantation
(Meeting Hall 1)

Concurrent Session 16:
Bringing Hearts Alice and Kicking
(Panorama Hall)

Concurrent Session 17:
B-Cells, Antibodies and Graft Injury
(Meeting Hall 4)

Concurrent Session 18:
AMR in Thoracic Transplantation: Are We Making Progress?
(North Hall)

1:15pm – 3:15pm
Lunch and Council Meetings

1:30pm – 3:00pm
Mini Oral Session 1:
Mechanical Circulatory Support
(Meeting Hall 1)

Mini Oral Session 2:
Heart and Pediatric

Rejection (AMR) and late complications that demand innovative immunosuppressive strategies.

The session continues with Dr. Paul E. Nolan, Jr. from Arizona, U.S. describing the pre-transplant journey of Advanced Heart Failure with BTT MCS and malfunction due to thrombosis. Dr. David O. Taylor from Cleveland, U.S. will address primary graft failure at week one. Attendees will better understand the various causes of early allograft failure and a clearer picture of the incidence, risk factors and outcomes of primary graft failure (as opposed to other causes of early graft failure). Main points will be the low but important incidence of early graft failure (EGF) with its high mortality and possible treatment options including MCS as well as re-transplantation. The final part of the lifecycle journey, Late Post-Transplant is addressed by Dr Michael Shullo, Pittsburgh, U.S. who will give a presentation entitled "Development of skin cancer and pre-cancerous colon polyp". The session will conclude with audience participation and discussions with the expert panel on best practices.

Preview: Tolerance is Not Overrated

Although the introduction of cyclosporine in the early 1980's led to significant advancements in organ transplantation, organ rejection still occurs. During today's **Concurrent Abstract Session 11: Tolerance, To the Bench and Back**, presenters explore alternative pathways to prevent rejection. During the invited lecture, Dr. Mohamad Sayegh discusses the importance of T-cell co-stimulation in an immune response. Presentation of an antigen to a T-cell without binding of a co-stimulatory molecule on the antigen presenting cell to its corresponding receptor on the T-cell leads to the development of anergy. This represents a potential avenue to induce tolerance as Dr. Sayegh reviews the current state-of-the-art and challenges the audience to develop new thinking involving T-cell tolerance.

Following this, four groups presented their research. Heim et al explore the role of attenuating the initial ischemic reperfusion injury in preventing chronic transplant atherosclerosis in a mouse model. Lendermon et al provide further evidence on the importance of the Th-17 immune response in the pathogenesis of obliterative bronchiolitis, by creating a T-bet negative mouse model. T-bet is a transcription factor that downregulates the Th-17 immune response. Salman et al report on the increased circulating regulatory T-cells believed to protect against rejection. Correlating with improved lung function after transplantation. Lastly, Derkatz et al report that infants have the highest levels of CD22+ B-cells. CD22 is an inhibitory B-cell molecule, leading to development of tolerance when the B-cell is exposed to an antigen. The authors hypothesize that this may explain why infants develop tolerance to foreign ABO antibodies more often than older patients.

Did You Know?

Charles University in Prague, named for King Charles IV, was the first University in Europe. It was established in 1348.

Johannes Purkinje, for whom Purkinje fibers are named, was a medical doctor and physiologist at Charles University in the 1800's.

Albert Einstein was a professor of physics at Charles University for a period of time.

Follow the ISHLT on Twitter!
@ISHLT

Stay connected at the ISHLT Annual Meeting this year by following us on Twitter - the real-time information network that connects you to the latest stories, ideas, opinions and news about what you find interesting.

If you already have a Twitter account, follow us! We will be tweeting before, during, and after the Annual Meeting in Prague, using the hashtag **#ISHLT2012**. Stay up-to-date on the latest news and events taking place onsite.

We encourage you to join our online conversation. Please tweet your reactions, comments, and interesting things you learn throughout the daily sessions at the Annual Meeting.

How to use our hashtag:

- At the end of every tweet, type **#ISHLT2012**. This will allow everyone to follow the conversations happening at the Meeting.
- On Twitter, search **#ISHLT2012** to read what your ISHLT colleagues are tweeting.

If you are new to Twitter and want to learn more about this online communication tool, below are some great info links:

https://twitter.com/about
http://mashable.com/guidebook/twitter/

If you need a **Tweetorial** (to set up a new Twitter account), please stop by the Press Room in Meeting Room 2.4 anytime during the Meeting. Our Press Room staff would be happy to help you start Tweeting!

REVIEW: Tearing Down Curtains

The opening plenary session was all about breaking down the walls. Dr. Lori West, who stated that there are over 2500 registrants, from all over the world, for this Annual Scientific Meeting. Dr. Jan Pirk, who started the first Czech thoracic transplant program, welcomed the crowd, and noted that after breaking the first wall, with the fall of the Iron Curtain, he first addressed the 10th Annual meeting of the European Association for Cardiothoracic Surgery, in 1996, at the Congress Center. Dr. Stehlik followed and reviewed the history of the Czech Republic. Dr. Walter Klepetko reminded us that despite the political walls, collaboration in the heart and lung transplant community has helped to break through the walls. He focused on regional cooperation between Austria and the Czech Republic that allowed the first lung transplant center to be established in Prague in 1997, and the further collaboration between Prague, Vienna, and surrounding Eastern European countries to allow patients in the area to undergo lung transplantation. The model of a central transplant hospital with regional referring facilities providing substantial post-operative care led to good outcomes and has given the opportunity for independence. This model should be considered in other parts of the world. The famed physicist, Lawrence Krauss, ended the session with the importance of breaking down another wall – the influence of politics on science. While he lamented various instances in which politics has trumped science in the United States, he stated that he was heartened by recent polls showing that Americans believe that policy be driven by science rather than politicians.

Million Dollar Man – Machine or Biology

What does the future hold for those suffering from end-stage heart failure? That was the big question of yesterday's **Pre-Meeting Symposium 07: New Devices, New Approaches,** chaired by Dr. Strueber and Dr. Park. An increasing number of patients are unresponsive to optimal medical therapy as defined by recent guidelines. The optimal treatment for refractory heart failure is cardiac transplantation. However, a profound shortage of donor hearts limits the use of transplantation as a solution to the expanding number of patients with advanced heart failure worldwide.

VADs have evolved significantly in the past 25 years, beginning with conversion from external to internal placement, conversion from pneumatic to electrical power and transition from pulsatile to continuous-flow devices. Two different systems in current use are - axial and centrifugal devices. Dr. Pagani compared these two techniques, pointing out that both have comparable positive results with differences difficult to assess. The preferred technique depends on the individual patient. New devices are on the horizon with new designs and improved hydrodynamic performances. Smaller devices, which only partially unload the heart with an average flow of 2.0 – 2.5 l/min are coming into clinical use. They can be implanted between the left atrium and right subclavian artery having good results. Dr. Griffith predicted that these pumps will be the dominant VAD of the future. However, there is change in indication.

Dr. Park presented data on patients who received an LVAD implanted in preserved systolic LV function. Patients with a restrictive cardiomyopathy on the transplant waiting list, the LVAD group, had a better survival than the group without LVAD. In addition, liver and renal function improved. Dr. Park wondered if this patient group will rise with the machine.

How does the future look? Machine Or Biology? In "The Future For A Patient With A Failing Heart Is With Machines", Dr. Kirklin stated that MCS has evolved in recent years as transplant alternative. Transplant patients without risk factors have better outcomes when compared to patients with risk factors. Patients with risk factors might profit from LVAD therapy instead of transplantation. Thus, the major challenges are accurate contemporaneous risk-adjusted depictions of survival after cardiac transplantation and MCS. The real challenge is to find common ground between transplantation and MCS analysis which accommodates differing patient populations. This will allow a paradigm to expand current concepts and strategies that follow a patient shift from one therapy to another with the focus on both long-term survival and patient satisfaction.

The frequency of adverse events such as thrombembolism, stroke, infection and death decreased with introduction of new VADs, making these devices suitable for larger patient groups. But adverse events can't be negotiated. "Machine or Biology? The Future For A Patient With A Failing Heart Is With Xenotransplantation," said Dr. McGregor. The advantages of a cardiac xenotransplantation are, no need for anticoagulation and no need for extrinsic power source. But before the treatment of choice for a patient with a failing heart is with xenotransplantation, hurdles must be overcome. Median survival after heterotopic cardiac

Transplantation
(Meeting Hall 4)

Mini Oral Session 3:
Pulmonary Hypertension and Lung Transplantation
(Meeting Hall 5)

3:15pm – 4:30pm
Concurrent Symposium 3:
Mechanical Circulatory Support – When is It Too Soon or Too Late?
(Congress Hall)

Concurrent Symposium 4:
Large and Small Vessels Disease in Heart Transplantation
(Forum Hall)

Concurrent Symposium 5:
Tough Situations in Cardiac Transplantation: Bring in the Experts
(Meeting Hall 1)

Concurrent Symposium 6:
Lung Transplantation for Pulmonary Arterial Hypertension – A Review and Panel Discussion
(Panorama Hall)

Concurrent Symposium 7:
Special Considerations: Cystic Fibrosis and Lung Transplantation
(Meeting Hall 4)

Concurrent Symposium 8:
Risky Business :Infectious Risk in Donors and Recipients
(Meeting Hall 5)

Concurrent Symposium 9:
Coagulation and Transplantation – The Clot Thickens
(North Hall)

5:00pm – 6:15pm
Concurrent Symposium 10:
Joint ISHLT/IPTA Symposium
(North Hall)

Concurrent Session 19:

MCS: Desired Outcomes – Can We Get There
(Congress Hall)

Concurrent Session 20:
Advanced Heart Failure: When is a Contraindication Not a Contraindication to Transplant
(Forum Hall)

Concurrent Session 21:
Therapeutics of Lung Transplantation
(Meeting Hall)

Concurrent Session 22:
Pulmonary Hypertension: Assessment and Prognosis

Concurrent Session 23:
Clinical Case Dilemmas In Thoracic Transplantation
(Meeting Hall 4)

Concurrent Session 24:
Heart Failure: Back to Basics
(Meeting Hall 5)

xenografts is now >90 days with clinically tolerable immunosuppression. The life sustaining orthotopic model is currently being studied with initial promising early outcomes, but present data do not yet justify clinical application.

"Machine Or Biology? The Future For A Patient With A Failing Heart Is With Stem Cells," explained Dr. Terzic. He reported from lineage-specified stem cell products developed for treatment of heart failure. The C-Cure clinical trial is a multi-center randomized trial that assessed autologous cardiopoietic stem cells in chronic ischemic cardiomyopathy. This Phase II trial documented feasibility and safety of cardiopoietic stem cells in ischemic cardiomyopathy. With a complementary standard of care, the cardiopoietic stem cell therapy improved cardiac function and clinical performance. Further pivotal studies are under way. However, stem cell therapy is presently no alternative to transplantation or MCS.

This extra-ordinary session ended with a discussion by panelists on the promising approaches for improved patient outcomes as they are identified and currently investigated.

REVIEW: Rejection is Never Easy

Yesterday's **Pre-Meeting Symposium 14: "The DEFs of AMR: Detecting the Antibodies, Evaluating the Biopsy, and Finally, the Patient"** was chaired by Drs. Allan R. Glanville and Jon Kobashigawa. It focused on advances in antibody detection, pathologic parameters for diagnosis and brought it all together with clinical correlation. As Donor-Specific Antibodies (DSA) are not always detectable in the blood of patients with AMR, AMR is solely defined by pathologic criteria. However, it is believed that the detection of DSA during AMR episodes might be associated with negative outcomes in these patients. Dr. Dolly B. Tyan compared IgG and C1q for the detection of AMR. Both (IgG+/C1q+) antibodies are associated with adverse outcomes for kidney and heart allografts. Patients with IgG-/C1q+ (IgM) antibodies that are donor-specific can also have an adverse effect on heart allografts and should be treated. IgG+/C1q- status has an as yet to be determined significance. Does it play a role in chronic rejection? In some cases, patients can seroconvert to IgG+/C1q+, but to date there are no data of its importance. Further exploration is needed.

Dr. Charles C. Marboe introduced the new pathology nomenclature and classification for AMR in heart transplant recipients based on histologic and immunopathologic findings. He discussed immunohistochemistry of C4d and C3d and presented data from the Cleveland group with a high sensitivity for C4d+ and C3d+ in AMR associated with an elevated adverse outcome in terms of cardiac allograft dysfunction and death. He went on to present the revised ISHLT grading of lung transplant pathology and acute lung rejection. In AMR of lung transplant recipients C4d seems to be important. In a study by Yousem et al. of 23 patients with new onset DSA and graft dysfunction, 74% had coexisting Acute Cellular Rejection (ACR). The recommendations for AMR are to have DSA with each biopsy or when C4d is performed. C4d staining should be performed among patients in high grade ACR (ISHLT grades A2 -4), acute lung injury or neutrophilic capillaritis, chronic rejection (B2R or repetitive B1R) and unexplained graft dysfunction. Let's come to the clinical correlate: "What Does It All Mean? What Are The Big Unanswered Questions?" Dr. Martin R. Zamora answered for the field of lung transplantation. Pulmonary capillaritis is often the clinical correlation of AMR, as seen by antibody depositions and production in biopsies of patients with pulmonary capillaritis after lung transplantation. The future needs are the natural history of preexisting and de-novo HLA antibodies as well as the role of non-HLA antibodies or anti-self antibodies. To date, the importance of complement fixation and the treatment of both symptomatic and asymptomatic patients with DSA remain unclear. The clinical correlate: what does it all mean and what are the big unanswered questions for heart transplantation? Dr. A.G. Kfoury familiarized the audience with the new 2010 ISHLT AMR nomenclature for endomyocardial biopsies. Implications of the change on clinical practice in heart transplantation were highlighted. Early screening for AMR is recommended, subclinical AMR was introduced and severity of pAMR graded. Possible treatment strategies for symptomatic cardiac AMR include high-dose steroids, thymoglobulin and change of maintenance immunosuppression. New strategies are in-progress. Some of the big unanswered questions in cardiac AMR are optimal treatment protocols of clinically-manifest AMR, surveillance and follow-up. Patients with asymptomatic AMR are not well characterized. To date, data on incidence, monitoring and optimal treatment protocols are missing. In summary, there is ongoing advancement of diagnostics and therapy of cardiac and lung AMR, but there are still ways to go to fully understand and effectively treat AMR.