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Schedule at a Glance
Friday, April 20

7:00am – 6:00pm

Registration Desk Open

8:00am – 9:15am

Concurrent Symposium 11:
Management of the Failing Fontan Patient Across the Age Spectrum
(Meeting Hall 4)

Concurrent Session 25:
VAD Future: Recovery and New Devices
(Congress Hall)

Concurrent Session 26:
Heart Transplant Immunosuppression: What Can We Learn From Clinical Trials?
(Forum Hall)

Concurrent Session 27:
Basic Science of Lung Transplantation
(Meeting Hall 1)

Concurrent Session 28:
Right Ventricle Function
(Panorama Hall)

Concurrent Session 29:
Role of Physical Activity in the Pre and Post-

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Curious Beginnings

According to Sherwin Nuland MD, a best-selling author, medical historian and Professor of Surgery, the roots of Pediatric Cardiology, Pediatric Cardiac Surgery, and all of Heart Surgery began with the so-called “blue-baby” operation, first performed on November 29, 1944 at the Johns Hopkins Hospital. If all of Heart Surgery can be traced back to Pediatric Cardiology, then Heart and probably Lung Transplantation must pay a special tribute to the pioneering work of Helen B. Taussig (1898-1986). Thoracic Transplantation began with her demand of Alfred Blalock (1899-1964), “we are going to have to build a *ductus*,” to treat Tetralogy of Fallot. Let’s not forget Vivien Thomas (1910-1985), the African-American surgical technician to Blalock whose schooling ended with high school, who pioneered a method of diverting blood and developed the atrial septectomy with an undetectable suture line like “Something the Lord Made.”



Preview: You Won’t be Able to Resist This Session

Concurrent Session 47 chaired by Glen P. Westall, PhD and Frauke Mattner, PhD deals with an important topic in organ transplantation and subsequent immunosuppression: “**Evolving Infections in a New Era**”. The session begins with a presentation by Dr. Minces from Pittsburgh, U.S. about Ganciclovir-resistant CMV infections in lung transplant recipients highlighting the need for prevention of CMV infections. The following discussion focuses on chronic CMV infection in high-risk lung transplant recipients. In a prospective cohort of eight D+/R- recipients, the CD4+ and CD8+ CMV-specific T-cell memory responses from BAL-obtained lung mononuclear cells and peripheral blood compartments during aviremic chronic infections were seen. The influence of different antiviral strategies and immunosuppressive therapies on CMV immunity was investigated by Dr. Petrisli and colleagues in heart transplant recipients. They found that reconstitution of CMV-specific immunity after heart transplantation is modulated by mTOR inhibition with everolimus, but not by antiviral strategy.

A group from Groningen/ Netherlands systematically analyzed chronic hepatitis E infections in lung transplant recipients and found that in 2% of their patient cohort having genotype 3, which is currently being recognized as an emerging zoonotic pathogen. Going from a therapeutic approach to a diagnostic approach in thoracic organ recipients a multi-center study in pediatric lung transplant patients evaluated the effect of deep-sequencing for the identification of viruses compared to multiplex-PCR. Invasive fungal infection is a life-threatening complication of lung transplantation. The last talk of this session will address risk factors for invasive fungal infection after lung transplantation, studied by an Australian-based group and presented by Dr. Chambers.

Small but Significant Steps

Tucked away in a corner of the poster hall, Dr. West and I found a poster we had hoped would be here... **Poster #904, "Impact of Evolving Organ Donation Practices on Lung Transplantation in China"**. Perhaps, as evidence of the difficulties the authors had to face to accomplish internationally acceptable organ donation practices in China and actually get here to present their work, the poster had fallen down. When we put it back up, we saw a description of how transplant has advanced, at least in one location in China, to provide transplantation without the use of executed prisoners.

The authors, Drs. W. Mao and J. Chen are to be commended for their effort to share this small but significant experience. We hope this small but significant step signals the onset of a real change for the organ donation and transplantation systems in China.

Transplant Setting
(Meeting Hall 5)

Concurrent Session 30:
*Innate Immunity and
Ischemia Reperfusion
Injury*
(North Hall)

9:45 am – 11:15am

Plenary Session
*The Aging Imperative:
Ethics, Economics and
Resource Allocation*
(Congress Hall)

11:45am – 1:00pm

**Concurrent Symposium
12:**
*MCS Recovery – How Do
We Get There?*
(Congress Hall)

**Concurrent Symposium
13:**
*The Leading Edge of
Immunosuppression in
Heart Transplantation:
Evidence, Perspectives
and Clinical Practice*
(Forum Hall)

**Concurrent Symposium
14:**
*Following the RV
Through Thick and Thin*
(Meeting Hall 1)

**Concurrent Symposium
15:**
*Solving the Enigmatic:
Cases in Heart and Lung
Transplantation*
(Panorama Hall)

**Concurrent Symposium
16:**
*Bad Bugs – What Can
We Do?*
(Meeting Hall 4)

**Concurrent Symposium
17:**
Pulmonary Hypertension



Preview: Bad Bugs, Whacha Gonna Do When They Come For You?

Infection is a major complication after heart and lung transplantation. With increasing virulence and/or resistance of many bacteria, it is easy to feel uneasy and one step behind. During Concurrent Session 16 on Friday morning, experts will tackle some of these clinical nightmares. Dr. Michele Estabrook will discuss *C. difficile*, including the recent outbreak of a hyper-virulent strain in many parts of the country. She will focus on prevention and new modalities of treatment. Dr. Stanley Martin will address VRE and MRSA, with an emphasis on the epidemiology of infection and treatment of these infections, especially in cases where standard therapy appears sub-optimal.

Dr. Frauke Mattner will discuss how to prevent the infections, or as she states it “get the bugs before they get you.” Dr. Stanley Martin will conclude with the ever-increasing problem of multi-drug resistant gram negative infections. He will discuss innovative approaches to addressing these infections, including the use of some old antibiotics, use of different doses and routes, and the complicated issue of combination therapy. This is a must-attend session for all transplant physicians.



PREVIEW: A Shift to the Right

After Dr. Krauss's talk during the opening plenary session encouraging a shift to the left, the researchers during **Concurrent Session 28** on Friday morning will encourage participants to shift to the right ... ventricle, that is.

Dr. Guihaire and colleagues will present two studies using a porcine model of pulmonary hypertension. Their first study will provide evidence that ventricular arterial uncoupling in response to pulmonary hypertension is a significant determinant of right ventricular size, systolic function, and right ventricular stroke volume. Their second study, which involves a porcine model of chronic thromboembolic pulmonary hypertension, found that reperfusion is associated with desired right ventricular structural changes on echocardiography, with histological evidence of decreased cardiomyocyte size and expression of beta myosin heavy chain protein. Dr. Haddad and colleagues will present evidence that septal curvature during both systole and diastole correlates with hemodynamic and structural characteristics in patients with pulmonary arterial hypertension.

Next, Dr. Stackhouse and colleagues will present evidence that echocardiographic features, specifically right ventricular size and the change in right ventricular size on serial echocardiography, are independently associated with mortality in patients with pulmonary hypertension. Subsequently, Dr. Rivera-Lebron and colleagues will present their research which underscores the importance of pulmonary hypertension, specifically right heart failure, as a prognostic indicator in patients with idiopathic pulmonary fibrosis. To close the session, Dr. Tudorache and colleagues will bring us back to left – they will present data that in patients with pulmonary hypertension and right heart failure, chronic underfilling of the left ventricle can lead to detraining of the left ventricle. With lung transplantation, decreased right ventricular afterload leads to increased pulmonary blood flow and increased venous return to the left side. The left heart may not initially tolerate this increased preload. The researchers address management issues including the use of bridging patients with veno-arterial ECMO.



Preview: Trending Now – Giving Small Hearts a Fighting Chance

Concurrent Abstract Session 45: **Growing Up with a Heart Transplant: Adolescence, Antibodies, and Pharmacogenetics** deals with pediatric heart transplantation and associated outcomes. The discussion will begin with pharmacogenetics of tacrolimus in pediatric heart transplant recipients by Dr. McLean. Dr. VanderPluym continues with “Is Adolescence an Independent Risk Factor for Rejection in Pediatric Heart Transplantation, Independent of Age at Listing?” in which data of 3,424 pediatric patients who underwent transplantation at 36 centers in the Pediatric Heart Transplant Study (PHTS) are given. The session shifts to Dr. Krishnamurthy describing the prevalence of academic, behavioral, and affective issues in pediatric heart transplant recipients 10 to 20 years post procedure. The following three talks will address antibody mediated rejection (AMR), which has been identified as a clinically important cause of acute and chronic cardiac allograft dysfunction. Dr. Zeevi evaluated the correlation between level of HLA-antibodies and the ability to bind complement (C1q) by a novel Luminex-based assay. Subsequently, Dr. Castleberry compares complement fixation by C1q and mean fluorescence intensity (MFI) for detection of clinically relevant antibodies. Dr. Irving will conclude this session with an analysis of transient and persistent donor specific and non-donor specific HLA antibodies (DSA) on graft outcome.



**REVIEW: B-Cells and Thoracic Transplantation:
The Good, The Bad, and the Ugly**

During Thursday's **Concurrent Abstract Session 17, B-cells, Antibodies, and Graft Injury**, the spotlight was on the B-cell. Dr. Richard Pierson reviewed the current state-of-the art about the role of B-cells in thoracic transplantation. First, the good – in patients with long term evidence of graft acceptance despite lack of immunosuppressive medications, there is an upregulation of B-cells. Second, the bad – the increasing recognition of antibody mediated rejection (AMR) associated with panel reactive antibodies (alloantibodies) and possibly even autoantibodies. Finally, the ugly – the role of B-cells in hyperacute rejection, due to anti-donor antibodies. This provides indirect evidence that B-cells may have a protective role in certain circumstances. Possible reasons include the importance of low, sub-injurious levels of antibodies in triggering cellular responses to protect it against further injury – what doesn't kill the graft makes it stronger. Following this, Dr. Mohanakumar presented data for a murine T-reg depleted model showing antibodies to both MHC class I and class II lead to obliterative airway disease (OAD). Administration of T-reg cells via passive transfer or neutralization of IL-17 attenuated the formation of OAD, suggesting that IL-17 is a mediator of OAD and that T-reg cells attenuate the injurious response. When non-complement fixing MHC antibodies were used, OAD still occurred suggesting complement mediated damage is not necessary to develop OAD.

Dr. Matsuda presented data that spleen tyrosine kinase (Syk) may contribute to the lymphoid neogenesis seen with obliterative bronchiolitis. Syk is involved in B-cell proliferation and B-cell receptor signaling. A murine intrapulmonary tracheal transplantation model in which a donor trachea was transplanted into the left lung was used. When compared to control mice, the Syk knockout mice had less graft occlusion and smaller lymphoid aggregates with almost complete absence of B-cells. Interestingly, fewer T-cells were present as well. These findings open the doors to future therapies for preventing obliterative bronchiolitis in the future.

Dr. Chruscinski presented data that antibodies other than anti-HLA antibodies may be associated with AMR after heart transplantation. They compared 12 patients with biopsy proven AMR with 19 control patients. Antibodies against IgG (rheumatoid factor), ribosomal P, tropomyosin, oxidized human LDL, ssDNA, endothelial lysate, and dsDNA were elevated compared to control patients. It is unclear whether these antibodies are the cause of the tissue injury or a result of sensitization from previous tissue injury. Of interest, patients with AMR were more likely to have had an LVAD.

Dr. Urschel presented research seeking to explain why infants have impaired responses to T-independent (TI) antigens such as blood group (ABO) polysaccharides. As a result of this impaired response, infants tolerate ABO incompatible heart transplantations. CD21 hi B-cells are important in response to TI antigens, and C3d binding to CD21 amplifies the immune response. Although infants have similar numbers of CD21 hi B-cells and similar levels of soluble C3d compared to older individuals, the investigators found that adult and infant B-cells have different downstream signaling after stimulation with anti-IgM antibodies in an in-vitro model. Using flow cytometry, they found that adults B-cells had upregulation of two downstream mediators phosphorylated SYK and AKT, both important in B-cell activation. However, stimulation of infant B-cells resulted in downregulation of AKT. Being able to translate these findings and modulate the response to TI antigens in adults may allow transplantation of ABO incompatible organs in the future.



PREVIEW: The Discipline of Managing Self

Transplantation is a chronic condition. Medical dependency is not eliminated and patients have to manage the therapeutic regime, life roles and emotions.

It has been suggested that the implementation of chronic illness management approaches might be the most promising pathway to enhance the long-term outcome. Self-management support is a key component of chronic illness management and has been associated with favorable clinical outcomes.

Self-management support entails more than traditional patient education. It entails strategies to develop problem-solving skills and to improve self-sufficiency. Moreover, support for self-management is embedded in a healthcare system that ensures access to and continuity of care, increasing opportunities for patients to participate in the care process and coordination of care between settings, which necessitate healthcare system changes into the direction of chronic care. **Concurrent Symposium 20: Self Management in End Stage Heart and Lung Disease and Transplantation** aims at clarifying the principles of self-management in heart and lung transplant recipients in view of managing the medical regimen, emotions and new life roles both in adult and pediatric patients in the context of chronic illness management.

in Chronic Parenchymal Lung Diseases: Does It Matter?

(Meeting Hall 5)

Concurrent Symposium

18:

Challenges in Pediatric Lung Transplant

(North Hall)

1:00pm – 3:15pm

Lunch and Council Meetings

1:15pm – 2:15pm

Concurrent Symposium

19:

Joint ISHLT/ESOT Symposium

(Meeting Hall 1)

1:15 – 2:45pm

Mini Oral Session 4:

Mechanical Circulatory Support II

(Panorama Hall)

Mini Oral Session 5:

Heart Transplantation

(Meeting Hall 4)

Mini Oral Session 6:

Lung Transplantation, Infectious Diseases and Donor Management

(Meeting Hall 5)

Mini Oral Session 7:

Basic Science and Immunobiology, Heart Transplantation and Infectious Diseases

(North Hall)

3:00pm – 4:30pm

Plenary Session

New Horizons

(Forum Hall)

5:00pm – 6:15pm

Concurrent Symposium

20:

Self-Management in End

Concurrent Symposium

31:

*Right ventricle – Staying
Alive*

(Forum Hall)

Concurrent Symposium

32:

*End Stage Congenital
Heart Disease:
Opportunities and
Challenges*

(Meeting Hall 1)

Concurrent Symposium

33:

*Stealing Beauty after
Lung Transplantation*

(Panorama Hall)

Concurrent Symposium

34:

*Fishing Lungs from the
Donor Pool*

(Meeting Hall 4)

Concurrent Symposium

35:

*Philip K. Caves Award
Candidate*

Presentations

(North Hall)

7:30pm – 8:30pm

**President's Cocktail
Reception**

Prague Municipal House



PREVIEW: LVAD, RVAD, Bi-VAD, BAD VAD?

During Saturday's **Concurrent Session 43**, moderated by Dr. Thomas Krabatsch and Dr. Heather Ross, presenters will focus on the significant challenges that patients with ventricular assist devices (VAD) face. Dr. Holman and colleagues present INTERMACS data which confirmed that pulsatile VAD had less durability than continuous VAD, which translated into lower survival at 12 months. Dr. Pajaro and colleagues will present data which showed that patients with Bi-VAD had significantly poorer survival to transplantation than LVAD. However, in contrast to many prior studies, patients with total artificial hearts (TAH) had improved survival compared to patients with Bi-VAD, even though the TAH patients were sicker. The survival of TAH patients approached that of patients with only an LVAD. Dr. Krabatsch and colleagues present some good news – in a review of 160 Heart Ware HVAD implantations, there was an overall low rate of adverse events.

Dr. Hubbert and colleagues report an innovative way of diagnosing pump thrombotic complications using daily sound recordings of the VAD which are transmitted by the patient via smartphone back to the physicians. If confirmed, this may enable improved monitoring and care of VAD patients, especially those who live far from the implantation center. Dr. Dhungel and colleagues report that patients with VAD have impaired sexual functioning after implantation, and detail possible reasons. Lastly, Dr. Segura and colleagues report on the effect of continuous flow VAD on the morphology of the ascending aorta, detected at the time of explantation or autopsy. Changes included fragmentation and depletion of elastic fibers, disorientation of smooth muscle cells, fibrosis, cystic medial degeneration and atherosclerosis. Although the current generation of continuous flow VAD has represented a significant advancement in mechanical circulatory support, this study suggests skepticism in fully embracing continuous flow VAD.



REVIEW: Bring Them On

Yesterday's **Concurrent Symposium 5 "Tough Situations in Cardiac Transplantation: bring in the experts"**, excellently moderated by Dr. Mandeep R. Mehra, was intended to stimulate a discussion between panelists and audience after presentations of two clinical cases presented by junior faculty members. And it did! Dr. Arezu Aliabadi presented the case of a 62 year old patient with diabetes and impaired renal function who was transplanted for ischemic cardiomyopathy. Over years renal function impaired slightly, immunosuppression was reduced and changed from calcineurin- to mTor-inhibitors, but the patient's renal function further declined to dialysis dependency. Indication and pre-operative risk factors such as diabetes and proteinuria have been discussed. What were the reasons for the impaired renal function? How to diagnose the underlying causes? Immunosuppressive regimens were addressed as well as timing of immunosuppressive switch in these patients. Dr. Hermann Reichenspurner outlining that changes in these patients are often "too little too late" and immunosuppression has to be on an individual basis.

The second case was presented by Dr. Jennifer A Cowger. She reported of a 45 year old patient with diastolic heart failure due to amyloidosis. ATTR (familial) amyloidosis was diagnosed. The patient underwent liver and heart transplant. Heart graft function decreased. Panelists discussed indications, timing, natural history and postoperative course of heart transplantation for cardiac amyloidosis. What are the reasons for the impaired graft function and how to treat them? Ethical issues have also been discussed in this regard. Dr. Sudhir S. Kushwaha gave insights to the Mayo Clinic experience and strategy for patients with amyloidosis.

All the panelists agreed that despite different center specific treatment strategies, yesterday's symposium clarified the careful selection of patients and treatment based on individual comorbidities are essential for achieving good results in heart transplantation. Well prepared and chosen cases as well as world leading experts in heart transplantation made this symposium, which was newly introduced this year, invaluable to the audience.

Editorial Note:

In Thursday's edition of the *Daily Links*, we printed the following statement in error "Charles University in Prague, named for King Charles IV was the first University in Europe." The statement should have read, "**Charles University in Prague, named for King Charles IV was the first University in Eastern Europe**". We regret the error and appreciate your continued support of *Daily Links*.