Contributing Writers: Shiwan Shah, DO Christopher Labos, MD Newsletter Contact: Lisa deLeon 972-467-9602

This issue of Daily Links sponsored by:



Dr: Defining and Refining your Diction, part 3

On a final parting note, among the best ways to sharpen your diction is to read extensively and peruse the dictionary. But before I bid you au revoir, I do not reluctantly expose the misuse of loathe for loath. Several different sessions on several different days by several different ISHLT members from speakers to the listeners confused and mispronounced loathe and loath.

The adjective loath (no e at the end) is a strong synonym of reluctant. When you are loath to do something (rhymes with both) you are reluctant nearly to the point of aversion. The verb loathe (loathe, rhymes with clothe) means to hate or despise. When you loathe the use of voriconazole without therapeutic drug monitoring or you loathe the use of C1q, C4d, C3d or MFI in detecting or validating AMR in lung transplantation you find these investigations disgusting or despicable. However, because of the lack of clinical validation you may more appropriately be loath to use these tests until their clinical use has been validated.

Consider paying attention to your diction and your choice of words. Your diction reflects who you are, the way you think, and the community (think microbiome) you identify with.

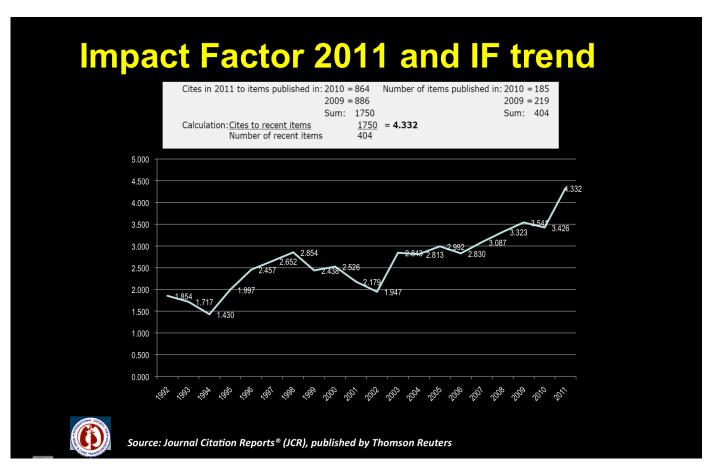
REVIEW: Strain is bad, but measuring it can't be bad

Most of us complain about the daily strain, but measuring strain in RV failure can help predict outcomes. Dr. Fine opened Friday's session on pulmonary hypertension by showing how RV free wall systolic strain can be easily done during routine echocardiography in PH patients and how it is linked to clinical outcomes. Similarly, Dr. Dandel presented evidence on RV strain parameters and their relationship to transplant free survival. However, Dr. Guihaire showed data that some markers typically thought to be related to RV contractility where related more to RV-PA coupling rather than contractility, at least in the pressure overloaded RV. Why the RV might behave differently in different etiological scenarios was underscored by Dr. Noly's presentation of how the transition to RV failure was delayed in PH patients compared to patients with PH due to chronic thromboembolic disease. All hope is not lost though. Dr. Verbelen's presentation on the hemodynamics of the RV after mechanical support was reassuring. Improving RV function is paramount, since imaging parameters such as septal dyssynchrony are independent predictors of clinical worsening.

REVIEW: JHLT Editorial Board Meeting

The JHLT Editorial Board met at noon on Thursday April 25th, 2013 to review the current health of the Society's journal. The JHLT has seen astounding impact growth (Figure 1) in the past few years and now ranks 1st among solid organ specific transplantation journals, 3rd among all transplantation journals and 6th in the field of respiratory medicine.

(Figure 1)



In the past 3 years, we have registered an 83% increase in submission of original research articles, enhanced the competitiveness (the acceptance rate for original articles is at 26%) and improved the decisional efficiency (time to first decision is 23.8 days) (Table 1). The papers with the greatest print citations and online use now include the INTERMACS mechanical circulatory support papers, original research with newer continuous flow devices as well as ISHLT guidelines, consensus and summary statements. The journal is well positioned to move into the digital landscape with availability on a variety of online portals including priority plans to develop a journal specific app on apple and android platforms. New changes for 2013 are depicted in Table 2.

Key Journal Accountability Metrics
Time to first decision (2013 metrics)

Submission to editor assignment – 1.7 days
Submission to reviewer invites – 3 days
Submission to First decision – 23.8 days
Average author turn around time for 1st revision – 41.4 days

In August 2013, we have convened a Journal strategic planning group to develop a 5-year strategy with the following goals:

- 1. Discussion around Journal name, its implications, positioning in the competitive landscape and threats and limitations of identity disruption
- 2. Digital interface and issues surrounding apps and seamless integration into social media portals; Future of the print journal
- 3. Strategy surrounding reaches and impact to non-members for the next 5 years

As always, the journal is indebted to the members and authors who put their trust in us for their important work, the readers, reviewers and society leaders.

(Table 2)

JHLT Changes 2013

• Additions

- New Section Editors – State of Art Series

- Basic Science for the clinician Series – Kim Gandy, Jim George (Coordinators)

- Audio slides (author developed voice content matched to figures and data)

- Online Video Content

• Category Adjustments

- Removal of Clinical Dilemmas (innovations and case anecdote categories remain)

- Case Anecdotes, Comment and Opinions

REVIEW: Making every dollar and every heart count

In tough economic times, people stretch every dollar. Transplant cardiology is facing tough times indeed since demand is greatly out stripping supply. A number of provocative studies examined ways this imbalance could be corrected. Dr. Khush showed that graft utilization is low overall and that the predictors of non utilization were not predictors of poor outcome. The suggestion being that liberalization of acceptance criteria might be indicated. However, a question from the audience challenge this view since the central European experience (which is much different than North American practice) has shown that lower quality donors hearts are associated with worse outcomes. Dr. Qader suggested that you can use a heart for transplantation even if the donor received CPR. Dr. Madden presented data from the UNOS database that donor hearts where the lungs had not been harvested paradoxically had better outcomes. Why this should be the case was the subject of much speculation. Dr. White presented two studies. The first dealt with donation after cirulcatory death, where RV failure long term may be due to RV distension following withdrawl of life sustaining therapy. The second study looked at the use of Hemopure, a donor blood alternative in an ex-vivo experiment, which provided superior preservation of myocardial energy metabolism. Finally, Dr. Esmailian presented the interim results of the PROCEED II trial looking at the use of a new OCS technology compared to cold storage to preserve donor hearts.



30th Annual Report ISHLT International Registry for Heart and Lung Transplantation – going purple?

Dr. Marshall Hertz has led the Registry for the past 11 years. His was an amazingly successful tenure, during which we saw an impressive growth in the depth of the reports and, we have also very much enjoyed his charismatic and plenary presentations. It is a privilege for me to take over as the new Registry medical director, and to present the 30th annual report.

There will be some changes that our members will see in the Registry work. In annual reports, we plan on exploring a defined topic in more detail, thus introducing a thematic focus every year. The 2013 report will explore age as an important donor and recipient variable. We have retired the old registry report logo, and we are introducing a new one. In my plenary presentation, I also asked for member input regarding a new 'ISHLT-purple' background for our slides. I thank all of you who have responded to my question – many responses arrived immediately and via twitter! So far the tally strongly favors purple ©.

I intend to work closely with transplant centers and country data collectives in regions currently not well represented in the registry, and hope to welcome new members to the ranks of Registry participants. The ISHLT Registry Booth in the exhibit area is available for on-site registration, and I will be happy to answer questions and help anytime after our annual meeting is over.

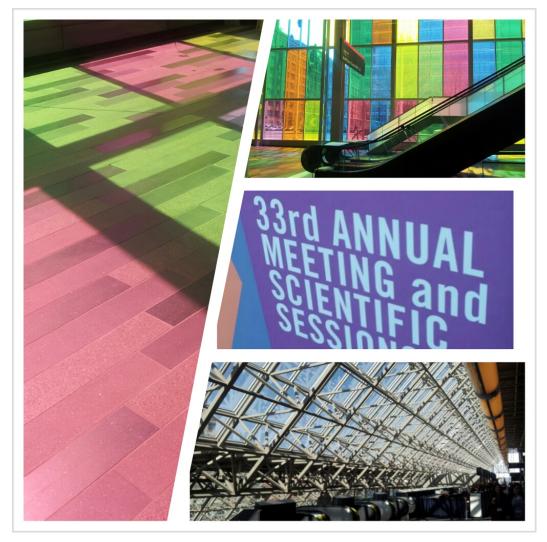
Finally, I would like to encourage members – junior investigators as well as their more seasoned mentors, to consider applying for the 2014 Transplant Registry Early Career Award. It is a terrific opportunity to participate in the Society's mission and to network with a group of terrific Registry Associate Directors. The submission deadline is January 2014.

I would like to thank you all for the opportunity to lead the Registry, and to thank Dr Marshall Hertz for showing me the way. Joseph Stehlik MD, MPH 4

PREVIEW: Mending an Achy Breaky Heart

As a pulmonary/critical care physician, I think the lungs are more important than the heart. However, all kidding aside, the heart is (one of the) most important organs in the body and thus it is only fitting that during the final plenary session of ISHLT 2013, speakers will take us from the bench to the bedside and discuss how to mend a broken heart. Dr. Jon Kobashigawa will start off with a review of the ISHLT Consensus Conference Report on primary graft failure after heart transplantation, including a review of the definitions, risk factors, and treatment. Following this, our ever-dynamic Dr. Mandeep Mehra will follow with a review of the ISHLT Consensus Report on 2013 Heart Transplant Listing Criteria. Dr. Marlene Rabinovitch will discuss novel therapies aimed at the bone morphogenic protein receptor pathway, shown to be important in idiopathic pulmonary hypertension. Dr. Mary Dew will discuss the importance of psychiatric distress with post-transplant morbidity and mortality. Last but not least, Emma Birks and Mariell Jessup will debate the use of VAD support as a bridge to recovery.

During the plenary session, two state-of-the-art abstracts will be presented. Gomberg-Maitland et al will present evidence that in the era of the lung allocation score, prediction models including the Pulmonary Hypertension Connection and French equation overestimate survival. This underscores the need for better prognostic models in order to better guide clinicians. Dunlay et al will present data on frailty and increased mortality after LVAD placement.



Palais des congres de Montreal

REVIEW: PH is No Laughing Matter

Despite the serious nature of pulmonary hypertension (PH), therapeutic options remain limited. During Friday morning's **Sunrise Symposium 7**, "**Proteins and Pathogenesis of PH**," the latest research on the cause of pulmonary hypertension was discussed. Dr. Sebastien Bonnet started off the discussion trying to convince the audience that micro RNA are involved in the pathogenesis of pulmonary hypertension, and that this may offer a therapeutic target in the near future. Dr. Ioana Preston discussed using techniques such as proteonomics and lipidomics to further insight into the pathogenesis of pulmonary hypertension. Conventionally, a hypothesis that a certain gene or protein is responsible drives the research. With these techniques, proteins and lipids are analyzed in a systematic fashion to identify targets that are expressed differently in PH versus normal patients. Once potential targets are identified, experimental models can be developed and tested. To end the session, Dr. James West discussed paradox of estrogen and PH. While females have a higher incidence of PH and estrogen has been epidemiologically linked to PH, in most animal models, estrogen has positive effects on the pulmonary vasculature. Estrogen is vasodilatory and anti-inflammatory, characteristics that should be beneficial. Based on a BMPR2 mutant mice model, Dr. West provided evidence that insulin resistance may explain this paradox. Estrogen contributes to insulin resistance, which may play a role in the development of pulmonary hypertension.

REVIEW: Under Pressure

Pulmonary hypertension (PH) often complicates lung disease, leading to worsening symptoms, with inconsistent responses to treatment. During Saturday morning's "Sunrise Symposium 11 – PH and the Lung Parenchyma, international experts will discuss PH in three different conditions. Dr. Steve Nathan will discuss PH in sarcoidosis, including information on prevalence, screening, and management. Dr. Jeff Golden will tackle the difficult topic of PH in scleroderma and will review recent trials and provide a therapeutic algorithm. Lastly, Dr. Martin Iversen will discuss PH in COPD and will provide attendees guidelines for which patients to treat and which patients not to treat.

REVIEW: Differing Opinions, Common Goal

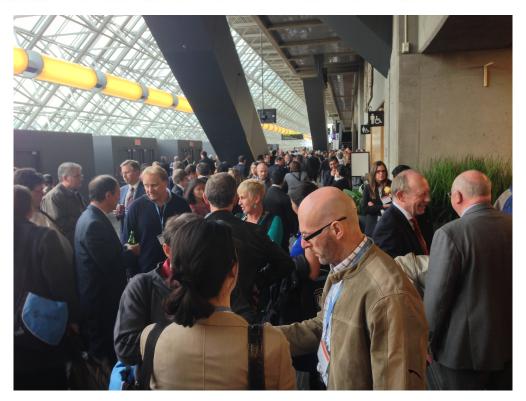
If you want three opinions, ask two cardiologists. Despite that usual joke, cardiologists generally agree about when to refer non-inotrope dependent patients for destination therapy, at least according to a survey from the CONSENSUS-DT trial, although the referral rates from INTERMACS suggest that there is a considerable gap between what cardiologists believe and what they do in practice. **Concurrent Session 37: MCS 9: Before the VAD** discussed part of the reluctance for referral may be due to the psychosocial stress, which is associated with decreased long-term survival post VAD implantation. Another adverse predictor of outcomes is renal replacement therapy at the time of implantation, which was also associated with adverse outcomes. The following presentation reinforced the link between cardiorenal syndrome and outcomes post VAD, suggesting that mechanical support should be implemented before the cardiorenal syndrome develops. Finally, just because everything had been too logical up to that point, Dr. Rame presented data on the lipid paradox showing that low cholesterol and triglyceride levels were associated with worse outcomes.

REVIEW: Pediatric Lung Transplantation: Developments and Controversies

During Saturday morning's **Sunrise Symposium 13, "Pediatric lung transplantation: development and controversies,"** experts tackled some recent development and controversies in the field of lung transplantation. One challenge that affects both the adult and pediatric population is the limited donor supply and consequently longer waiting times for some patients. Attempts to address this include the use of donation after cardiac death (DCD) for lung transplantation and the use of extracorporeal support as a bridge to lung transplant. There is expanding data in the adult population regarding the utility of these techniques and Drs. Melinda Solomon and Nicolaus Schwerk evidence for the use of these techniques in the pediatric population. Dr. Melinda Solomon discussed DCD and provided some promising data in the pediatric lung transplant population both with and without ex-vivo lung perfusion. Dr. Nicolaus Schwerk discussed the expanding use of veno-venous ECMO as a bridge to transplant.

Next, as anyone reading the pages of the Journal would know, there is fierce debate on the use of surveillance bronchoscopy in lung transplantation in general. Dr. Albert Faro brought this debate to the pediatric population. While he presented data that there was approximately a 20% incidence of asymptomatic rejection grade A2 or higher, almost all of these studies were in patients on cyclosporine based immunosuppression regimens. Although bronchoscopy is generally safe, there are complications, and it is unclear whether these data are still relevant in the tacrolimus era. The few studies with patients on tacrolimus based regimens indicate a lower incidence of asymptomatic rejection. Lastly, he discussed the use of cryobiopsy, a promising tool that allows one to obtain much larger samples than conventional transbronchial biopsies. This is sure to please pathologists and may revolutionize diagnosis of acute rejection as well as other lung transplant complications.

Lastly, Dr. Christian Benden discussed current concepts of therapy for chronic lung rejection, most based on the adult literature, including, augmentation of immunosuppression, the use of tacrolimus and mycophenolate as opposed to cyclosporine and azathioprine, the use of everolimus, and azithromycin



REVIEW: Predicting the Future, One Patient at a Time.

One of the many quotes attributed to Hippocrates is, "I believe that it is an excellent thing for a physician to practice forecasting. He will carry out the treatment best if he knows beforehand from the present symptoms what will take place later."

It is no wonder that we spend so much of our time trying to decide who amongst our patients will do well and who will not. Most cardiologists will not refer HIV patients for VAD implantation even though their prognosis is similar to non-HIV patients, presumably because they assume their prognosis is poorer. A new risk score that predicts the wait time for transplant was presented during the next presentation. The implication of course being that patients with a long predicted wait time should be receiving bridging therapy with mechanical support. Along a similar track, what followed was a presentation showing various risk factors that suggested transplant candidacy versus palliative care candidacy. Data was presented at **Concurent Session 42: Heart 10:**Can we improve transplant risk and assessment that patients with heart and renal failure did better with a heart and kidney transplant rather than just heart alone. In fact, those who received a heart and kidney transplant did roughly as well as those with no renal dysfunction who received only a heart transplant. There was evidence that elevated BNP and dilated left ventricles are unsurprisingly associated with worse outcomes. Finally there was some reassuring evidence that using VAD as a bridge to transplant may be cost effective.

Although we may not be able to predict the future as Hippocrates would like, we can least be proud that advances are being made to determine those factors most closely related to patient outcomes. That will hopefully allow us to "carry out the treatment best."

Curious about the award winners?

Check out the 2013 Award's Presentation on the ISHLT website:

http://www.ishlt.org/ContentDocuments/2013 Awards Presentation.pptx

REVIEW: A Child's Chest of Problems

During Concurrent Session 45, "Peds 3: Heart and Lung Transplantation," researchers presented some interesting studies in pediatric heart and lung transplantation. Irving et al started off by presenting data in an attempt to answer what to do when a pediatric cardiac transplant patient develops a donor specific antibody (DSA). Reviewing 108 patients, they found that 76% of patients developed a DSA, mostly class II, before development of complications including cardiac allograft vasculopathy, rejection, or graft loss, with a lag time from development of antibodies to development of complications of between 1.7 and 2.8 years. They suggest that once DSAs are detected, increased surveillance for adverse events should be implemented.

Ling et al presented data that CD1d+CD5+ B cells, which are immunoregulatory and produce IL-10, may be one of the reasons for better graft acceptance in infants. In a mice model, they found that in response to T cell dependent stimuli, IL-10 levels were increased, and proliferation of B cells was decreased. Further confirmation of this may allow for immunomodulation in older children and adults to improve graft acceptance.

Jacobsen et al presented data that CMV can predict CMV viremia specific T cell responses and that monitoring the T cell response can allow for altering immunosuppression and reduce CMV infection.

Goldfarb et al presented data from the UNOS database showing that adolescent's cystic fibrosis (CF) patients had worse outcomes than other age groups including adults. While transplants in this population are rare (14% of all CF transplants), outcomes were significantly worse, even when adjusting for confounding factors. The median survival in this patient population was 3.7 years, compared to 4.9 and 8.7 years for young adults (19-30 years) and older adults (31-50 years), respectively. This underscores the need for research into improving outcomes after transplant, as well as aggressive supportive care to try to delay lung transplantation as much as possible.

Continuing the opening plenary sessions of the microbiome, Sagar et al provided evidence that changes in the microbiome affect lung transplant outcomes. They evaluated 21 pediatric lung transplantation patients who underwent surveillance bronchoscopies and bronchoalveolar lavages during their first year after transplant. Patients who developed bronchiolitis obliterans syndrome (BOS) had overall decreased bacterial diversity compared to those who did not develop BOS. This further adds to the literature that reduced bacterial diversity is associated with complications in lung transplantation.

Khan et al presented data on pediatric thoracic multiorgan transplantation (TMOTx) using the UNOS database. Reviewing 2102 procedures, they found that except for heart-lung transplantation, survival for TMOTx was similar to heart only transplantation. While heart-lung transplantation was associated with worse outcomes compared to heart transplantation, survival was similar to lung transplantation. These data provide support for TMOTx in the carefully selected pediatric patient.

Thank you to all the writers, contributors, attendees, staff and everyone who made this event possible!

2013 Daily Links Editorial Staff:

Lisa deLeon, Stephen Chavez, Vincent Valentine, MD, Susie Newton, Shiwan Shah, DO, Christopher Labos, MD

Tweets from Twitter Tweeters...





Tweets from Twitter Tweeters (cont.)...



The ISHLT @ishlt

20h

Largest ISHLT meeting in history at 2,817 registrants! Thank you to all members, attendees and staff. #ISHLT2013 ow.ly/i/1YS9F

View photo



Diego Delgado @DrDiegoDelgado

9h

#ISHLT2013 great session on LVAD quality and life and cost @ishlt Are LVAD cost effective?

Followed by IHLH and 1 other

Expand ← Reply 13 Retweeted ★ Favorite ••• More





Laneshia Thomas @LaneshiakThomas

2

Had an aha! moment in the AMR session yesterday. I'm getting there. #ishlt2013

Expand



David Baran @davebaran Amazing PAH talk now at #ishlt2013 Truly amazing 1h

Followed by Kimberly Gandy and 1 other Expand