



April 7, 2017

DAILY *Links*

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

I smoke two joints in the morning/ I smoke 2 joints at night/ I smoke two joints in the afternoon/ And it makes me feel alright

Review Symposium 18

Weeding Out Fact from Fiction- the Highs and Lows of Marijuana Use in Transplant

The symposium started off with an informative yet entertaining presentation by Robert Page, PharmD, MSPH on the Pharmacology of a Weed. He first provided a quick history list full of fun facts about the history of cannabis dating back to when people were "Getting Stoned in the Stone Age." Of course in 1492 Christopher Columbus brought the plant to the English Colonies and the drug has been linked to numerous other famous figures since that time including George Washington and Queen Victoria.



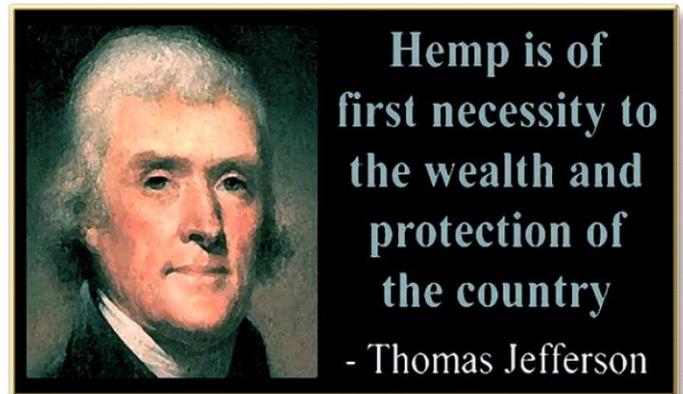
Next the audience received a lesson in '**Weed 101,**' where Dr. Page reviewed the endogenous cannabinoid system, which is responsible for modulated homeostasis. CB1 receptors found in the nervous system, connective tissues, gonads, and organs and is activated by the plant cannabinoid THC as well as the endocannabinoid neurotransmitter, anandamide (which looks very similar to THC).

Additionally, CB2 receptors are found within the immune system and are activated by cannabidiol (CBD). Finally, cannabidiol (CBD) doesn't have a very strong affinity for either CB1 or CB2 receptor but instead suppresses the enzyme responsible for breaking down endogenous anandamide (natural THC). Therefore CBD has low psychological inhibition with fewer side effects and is considered to be the primary target for medical applications.

How do we capture the medical benefits in a deliverable medication to patients? Several formulations have been studied including administration to the lungs (smoking or vaping), oral formulations, or topical applications. The pharmacokinetic parameters for each type of formulation are variable. In fact smoking marijuana has such a high bioavailability that the effect would be similar to giving the drug IV. Additionally, the

heat associated with vaping increased the temperature, which allows for even more THC absorption.

Finally, what are the concerns? First, with the drug not being regulated by the FDA there is high variability in packaging and labeling that may result in unintentional overexposure. Also, there is currently no regulation regarding purity, so there may be contaminants such as insecticides, fungicides or even molds (i.e. *Aspergillus*) on the leaves causing problems if inhaled. Additionally, THC, CBD, and CBN all interact with various Cytochrome P450 enzymes. In fact, CBD is a very potent inhibitor of CYP 3A4, 2D6, and P-glycoprotein (P-gp), which are all very important enzymes for the metabolism of immunosuppressant drugs. Inconsistent use of CBD will lead to inconsistent immunosuppressant levels and ultimately put the patient at greater risk of rejection. Finally, withdrawal from marijuana can have several worrisome symptoms including insomnia, depression, nightmares, anxiety, headaches and night sweats that may last from days to months. But who are we to disagree with Thomas Jefferson?



Dr. Patrick Smith, public health expert states the limited information available makes it difficult to determine its safety. Many varied opinions make it difficult to determine if it is safe or not to proceed with transplant listing. It's controversial to use cannabis for anxiety when one of the number one side effects is actually anxiety. There is high risk of depression with uses so in combination with prednisone you have a true winner! Additional side effects include memory loss. This puts the patient at risk of rejection. Will they forget to attend their appointments or take their medications? Although on the flip side the use as an appetite enhancer is beneficial. Additionally cannabis is arguably safer to use than opioids, as the risk of mortality is high. Long-term use is generally ill advised.

Lianne Singer from Toronto, Canada cites a 2016 poll revealing the prevalence of cannabis use in post-transplant patients: 7.4% in lung and 14.2% in heart. Their uses were for anxiety, sleep, mood etc, which shockingly are all side effects of the use. Marijuana smoke is very similar to nicotine. Longer exposure is associated with airway inflammation, bronchodilation, lower specific airway conductance, and lower FEV1 although studies vary. Some benefits may include antitumor properties in experimental models with the use of THC. In one case study lipid pneumonia was mistaken for CMV on a lung transplant patient. One recent study published in 2017 showed no significant difference in outcome on the recipients with the cannabis using donors versus those that don't although the research is limited. Cannabis has a high infection risk, which a recent study in Toronto showed legionella and aspergillus infections. In 2003 JAMA published a study on cannabis and immune function decreased lymphocyte assay for

The Smarter the Better? Smarter Pumping

Preview Sunrise Symposium 13
Interface of Design and Outcome

Is mimicking nature the solution for ridding adverse events in mechanical circulatory support? Despite the advances of ventricular assist devices over the past decade they remain limited by the significant incidence of adverse events. In this session approaches to understand and limit the problems of thrombosis, bleeding and infection will be addressed. This session will be chaired by Ulrich Steinseifer, PhD, and Robert L Kormos, MD. It focused on the role of system component interfaces in a presentation given by Marvin J Slepian, MD, and continues with a talk by Mark Slaughter, MD about smart monitoring and alarms using pressure sensors and data mining techniques. Francesco Moscato, PhD, will evaluate if it is possible to anticipate adverse events. The session will close with by J. Yasha Kresh, PhD presenting "Design/Interconnected Thinking for Better Biomedical Devices."

Knocked up?!?! I think NOT! Or maybe?

Preview Sunrise Symposium 16
Pregnant – Scared? So Are We

With advancing therapies, the impossible may now be possible. Women of child bearing age account for a large portion of the post-transplant population. In the past, it was advised to not get pregnant post-transplant with contraceptives or sterilization was recommended. Although the option to conceive post-transplant is multi-factorial. Consider the risks: CAV, antibodies, immune system, current immunomodulator therapies etc. This topic is very controversial. Is this putting the fetus at risk for being a motherless child? Little research has been done in this arena. Don't miss this hot session in the early hours Saturday morning Sunrise Symposium 16 at 7 am. Grab your cup of Joe and sip while you learn how to make possibilities be an option for some of your patient populations.

The Micro (Biome) Bubble

Preview Sunrise Symposium 17
Living in a Bacterial World: Microbiome in Thoracic transplantation

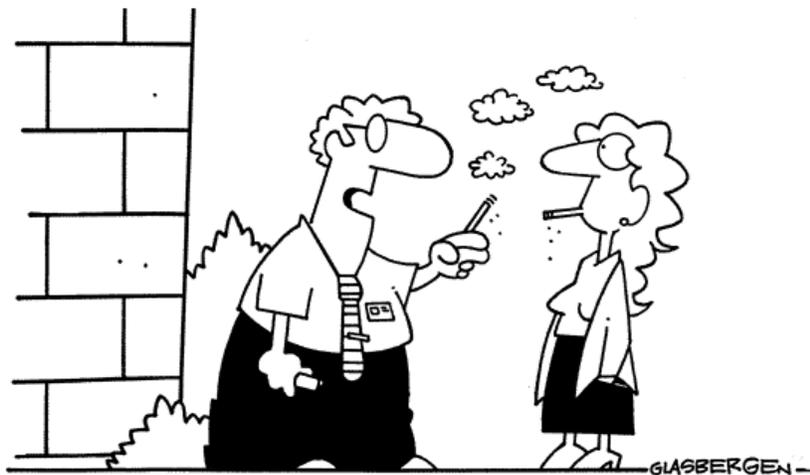
Germ. Bugs. Pollution. Transplantation. Antibiotics. Immunosuppression.

In one of the last sunrise session's of this ISHLT meeting, basic science and translational research in relation to the microbiome will be brought together by Bryan Coburn, MD, PhD, and Howard Eisen, MD.

Wilson Tang, MD, will kick off this session with an overview of the microbiome in health and disease. Followed by Maria-Luisa Alegre, MD, PhD, who will focus on the microbiome specifically in transplantation. Moving further to cardiac transplantation by Kiran Khush, MD, and then Sangeeta Bhorade, MD, who will concentrate more on the lung in relation to the gut. The main question to be answered will be: What's the role of the microbiome in affecting post-transplant outcome in the cardiothoracic transplant population?

Is it all bad? Although changes in the microbiome might be associated with negative effects on outcome in the transplanted patient, changes in bacterial and viral microbiome might be used to reflect extent of immunosuppression, and may facilitate modulation of immunosuppression and thereby outcome. So get yourself together for the last day of this ISHLT Meeting to step into the micro(biome) bubble of cardiothoracic transplantation.

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"I'm out in the fresh air and sunshine, my lungs are getting plenty of exercise and I'm consuming a leafy vegetable...this has to be good for me!"

UNDER PRESSURE: Controversies in Pulmonary Hypertension

Preview Symposium 28

Great Debates in Pulmonary Hypertension

You won't want to miss this exciting debate as some of the top experts in PH take the hot seat to deliberate a few of the most controversial issues in the field. Chaired by Teresa De Marco, MD, FACC and Paul A. Corris, MB, FRCP, this session will begin with Dr. Christopher King introducing a controversial case of Group 3 PH treated with pulmonary vasodilators. Next Dr. Steven Nathan and Dr. Marius Hoeper will argue for and against the treatment of PH due to lung disease with PAH specific therapies. What is the data to support or refute this? Is it true that some PAH specific therapies may worsen the underlying disease state?

Next up, Dr. Richa Agarwal will present a case of borderline PAH. Should patients with borderline PAH be treated with PAH specific therapies? Dr. Bradley Maron will argue that potentially earlier risk stratification and treatment of borderline PAH may improve outcomes. Dr. Jean-Luc Vachery will attempt to refute Dr. Maron's case by pointing out that borderline PAH is not PAH and we have no data to support treating this pre-disease state.

Finally, Dr. Roberto Badagliacca will introduce a patient case in which the patient has clinically stable PAH on monotherapy. Dr. Rogerio Souza will contend that despite being stable on monotherapy, the patient should still be escalated to dual or triple therapy to

optimize outcomes. Of course, this argument cannot go without dispute. Dr. Veronica Franco will point out that adding additional therapies may not be the 'bang for the buck' one would expect as there are many other factors to consider. With topics this controversial, the presenters definitely have their work cut out for them, **NO PRESSURE!**

Seeking the Magic Bullet

Preview Oral Session 25

Improving Outcomes in Pediatric Lung Transplant

This session aims to highlight novel approaches to get closer to the finish line of improving outcomes for pediatric lung transplant patients. Satoshi Ueda, MD, will share some of the challenges and long term outcomes after living donor lobar lung transplantation (LDLLT) using a single donor. Stuart Sweet, MD, PhD, will discuss findings of a prospective study in the pediatric lung transplant population looking at the impact of respiratory viral infections on outcomes. Igor Tudorache, MD, will present a novel treatment approach and a unique chance to study ischemia and reperfusion injury thru autotransplantation of the left lung in the setting of life threatening pulmonary hemorrhage. Evan Ammerman will be looking at the risk and outcomes of pulmonary fungal infection in this population. Joshua Blatter, MD, MPH, will dive into how anellovirus can be used to predict short and long term outcomes. Rachel Vanderlaan, MD, PhD, will conclude the session by sharing a single center perspective on the use of ECLS in pediatric lung transplant patients.

Coming Attractions

Rise and Shine!

No matter your field of interest, be sure to attend Sunrise Symposium 12 tomorrow morning, "HIV and Transplantation: It Isn't Going Away." Not only will you learn about end-stage heart and lung diseases associated with chronic HIV disease, but you're sure to gain insight into management of these issues in transplant recipients. Not to be missed!

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Plenary Session Live Stream Event

Join us live for our 3 plenary sessions this week for stimulating conversations and lively debate.

For free registration [click here](#).

CARVs and Zika and Mycobacteria, Oh My!

So much to do, so little time today!

Yogurt in hand, I started the day at Sunrise Symposium 6, "Those Darn CARVs: Community Acquired Respiratory Viruses in Lung Transplant." Erika Lease set the stage with a review of the epidemiology of respiratory viruses and CLAD, and Tereza Martinu continued with a discussion of pathogenesis and host responses leading to CLAD following CARV infection. We quickly learned that we have more questions than answers (a frequent theme in transplant ID) as Allan Glanville highlighted the limited evidence to guide therapy for CARVs. Never fear, though! Christopher Ensor discussed potential new therapies in the pipeline. Something tells me we'll have more to say about CARVs next year!

I continued my travels from the Midwest to San Diego at Symposium 16, "Around the World in 80 Days: Infectious Challenges in Cardiothoracic Transplantation." Having fielded numerous questions about Zika virus over the past year, it was exciting to hear Silvia Campos' as she described the (fortunately) few cases of Zika infection in transplant recipients. Emily Blumberg then gave an exciting and thorough review of hepatitis B in thoracic transplantation. Drs. Swaminathan and Sole masterfully tackled the challenges of latent and active TB in heart and lung transplantation, and I finished with pearls of wisdom for the traveling transplant recipient.

After a short break, I was reminded of the Ten Things I Hate About You, *M. abscessus*! at Symposium 23, "Taming of the Shew: *Mycobacterium abscessus* in Lung Transplantation." Cameron Wolfe discussed the epidemiology and modes of transmission of the pathogen, as well as implications for infection control measures. Orla Morrissey then described the challenges of diagnosing *M. abscessus* infections, as well as the need for non-culture based techniques. Fernanda Silveira provided thoughtful guidance on the pre-transplant management of patients with *M. abscessus* infection and colonization, and Patricia Ging followed with a discussion about therapeutic agents for these infections. In ISHLT-style grandeur and showmanship, Gregory Snell and Paul Corris provided wittily debated Australia vs. England (with a touch of *M. abscessus*). The jury is still out about the safety of transplant patients with this infection, but I certainly have a lot to chew over on the flight home Saturday morning...

Above and Below the Diaphragm, Let the Battle Begin

Review Symposium 12

A Tale of Two Organs: Selecting and Managing Multi Organ Transplant Recipients

John Dunning opened with a review of RV dysfunction and raised the question: "how bad do the ventricles have to be for consideration of combined heart-lung transplant?" Two rousing pro-con debate sessions followed, discussing combined heart-kidney and heart-liver transplants.

Eugene De Pasquale took up the banner for the pro heart-kidney position. He discussed the fluid definition of what makes a kidney truly vulnerable and shared data that showed patients who required dialysis after heart transplant alone had increased mortality compared to patients who received a combined heart-kidney transplant. Marcelo Cantarovich used a series of case studies and results from a Canadian consensus meeting to advocate for a staged heart-kidney approach.

Next into the ring were Sudhir Kushwaha and Charles Canter to debate on heart-liver transplants in patients with bridging fibrosis. Sudhir discussed the long-term survival benefit seen in the setting of combined organ transplant, while Charles shared a strong single center experience of patients with positive imaging findings and/or fibrosis on biopsy who underwent heart transplant alone. While a small sample size, none of the patients in that group have shown any decline any liver function. Richard Daily shared some of the challenges that come with post-op management of patients receiving a combined thoracic and abdominal transplant such as fluid management, immunosuppression regimens and induction therapies.

In closing, Heather Ross took on a formidable debate candidate - herself - to discuss the ethical principles that surround multi-organ allocation. 'While we are all charged with being good stewards of a very scarce resource, we must remember to balance individual justice with overall population utility.'

At the end of the session, the only losers here were the audience members left standing at the mic who weren't fast enough to be at the front of the line to get their questions answers before the session reached it's time limit.

Special Submission

Review Mini Oral Session 7

Factors that Drive Success in MCS

Left Ventricular Assist Device Implantation in Marijuana Users

According to Parijat S. Joy, the lead author of this study:

We did a retrospective analysis of over 20,000 hospitalizations for left ventricular assist device (LVAD) implantation, to compare complications and mortality in patients who had used marijuana, versus those who did not use marijuana. We found no significant difference in the rate of complications or mortality between the 2 groups. On adjusting for other patient related factors and accompanying other drugs of abuse, cannabis use was not associated with an increased risk of any complication or mortality within the duration of hospitalization. In conclusion, outcomes of hospitalization for LVAD implantation, in prior marijuana users is no worse than non-users of marijuana.

Overall success, but not one size fits all!

Review of Symposium 20

ECMO in Lung Transplantation: Sensational Success or Fantastic Failure?

Thursday's afternoon session, chaired by Erika Berman Rosenzweig, MD, and Reda E. Girgis, MD, on ECMO before or after lung transplantation gave a state-of-the-art overview of current ECMO technology, including cannulation strategies, patient selection, peri-operative and program management. Martin Strueber, MD shared his experience with different ECMO cannulations and configurations and discussed advantages and disadvantages from one technique over the other. Clemens Aigner, MD gave insights into identification of the right candidate, technique and timing for elective ECMO implantation which is always challenging with regards to a risk/benefit calculation. Sometimes a lung transplant candidate is in need of ECMO as an urgent bridge to transplant. Gregor Warnecke, MD shared his large experience with this strategy. Sometimes postoperatively ECMO is needed for rescue therapy. Göran Dellgren, MD highlighted the role of ECMO therapy for this indication with tips and pitfalls.

Is ECMO therapy a bridge over troubled water? David Michael McMullan, MD answered this question and indeed an ECMO program can be an overall success, but only if technique and setup is tailored to the individual patient.

A few reasons why ISHLT attendees should come to the Early Career Scientist Award in Transplantation to hear about the Human Respiratory Virome

4pm - Friday 7 April in Seaport F-H rooms

According to Alicia Mitchell, one of the finalists:

- The Virome is an emerging, exciting area of research and this presentation explores the translational aspects of basic virological laboratory research and clinical outcomes in Lung Transplantation
- This study is the first to ever describe a prospective, longitudinal analysis of the Virome (viral component of the microbiome) in Lung Transplant recipients

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