IMAGINE PRAGUE: A TASTE OF ISHLT APRIL 2012
Tereza Martinu, MD

I’ve been thinking of a better way of giving you a glimpse of Prague than just regurgitating some travel guide info. So… let’s do this:

Imagine Prague, April 2012. It’s Thursday, April 19th, you decide that you have learned enough about heart/lung transplantation, and it’s time to venture into the city. You manage to navigate the Czech signs and find the subway and make your way to the “Staromestska” (Old Town) station. You resurface on a busy street full of business-like men and women rushing back to work from their lunch break and students, walking to the nearby campus of Charles University, the oldest university in Central Europe. You follow the signs to the Old Town Square and manage to walk into ten people as your gaze is fixed upon the intricate facades of the City Hall and the bell towers of the imposing St-Nicholas church. You arrive in front of the medieval Astronomical Clock (Orloj), just as a group of people starts gathering there, all staring at this only working astronomical clock in the world, made in 1410. And then you realize that it’s 2PM: the skeleton statue next to the clock starts striking the time as the statues of the 12 apostles walk out of one window and back into the next above the dial. Congratulations, you have just witnessed the hourly Orloj ritual.

Then you walk towards the Vltava river (a.k.a. the Moldau). The view is truly astounding. The castle rises between dozens of towers on the other side of the river. You think to yourself: there is a good reason why Prague is also known as the city of one thousand spires. You walk across the Charles Bridge, between the two alleys of 30 imposing baroque-style statues, the Saints of all ages. Artisans, traders, and painters try to sell you trinkets, jewelry, souvenirs, and paintings of Prague.

Having crossed the bridge, you duck into a little pub. “Pivo, Mr/s. XYZ?” says the barman. Hearing your name, you automatically answer “yes” and only then wonder how on earth this barman knows your name. Profoundly embarrassed, you realize that you forgot to remove your ISHLT conference nametag. By the time you discretely hide your tag underneath your coat, a pint of Kozel is standing in front of you. You faintly remember what your Czech friend tried to teach you before you left home: “pivo” means beer and some small pubs have only one of the bizillion Czech beers on tap. You completely forget to look at the signs in the window to figure out which one they are serving here, although you’re not sure it matters, since the more Czech beers you try the more you are convinced that there aren’t any bad ones.

After your refreshment, you make it back to the streets. Since having emerged from the subway station, you keep noticing the elaborate and ornate sewer covers, decorated with the city coat of arms or the Czech lion crest. “How odd,” you think to yourself, “that this city prides itself in its architecture so much, it even decorates its manhole covers.” As you give in and take pictures of one such sewer cover, you feel observed from all sides and think, “the locals must be so used
A concept frequently invoked during philosophical discussions on caring for patients is the duality of art and science. Critical decisions under crisis situations demand this duality. For patients with a failing heart or failing lungs critical decisions abound. The ISHLT provides us bedrocks of principles which enhance our abilities to make better choices. We have yet not enough science, therefore the art of decision-making becomes crucial, especially under dire circumstances, first responders to the Twin Towers during 9/11.

The duality of art and science could be traced back to Heraclitus of Ephesus and Parmenides of Elea from Ancient Greece. These pre-Socratic philosophers planted the seeds of reason allowing other philosophers to propagate ideas across centuries of thought and investigations on how the world works. Heraclitus noted the universe is constantly changing. He claims “one cannot step twice into the same stream.” The world does not stay constant, like a flowing river, it is always changing, unless of course there are drought conditions, Texas today. It may be impossible to achieve true knowledge. Things we thought we knew are no longer the same when reexamined. Also, Heraclitus points out that things in existence are characterized by pairs of contrary properties, art and science. In the science of clinical medicine, confirmation relies on repeated studies showing similar results. Yet sometimes we repeat the same thing over and over expecting a different result, insanity?

Parmenides, on the other hand, argues that the world is an infinitely large and unchanging entity that misleads our senses. He explains change is impossible and existence is timeless in “the way of truth.” Parmenides concludes that knowledge
is gained through reason and not by the senses. The universe around us does not change, we change.

We need science, we need art, and we need the combination. A splendid example of this combination is experienced in the movie, Shawshank Redemption. Red, played by Morgan Freeman, represents the art of decency and Andy Dufresne, played by Tim Robbins represents the science of decency. Andy is methodical and patient about planning his escape to freedom as the two characters befriend each other through solace and redemption at Shawshank.

On a more comical note, the movie, Trading Places exemplifies other applicable dualities, nature vs nurture or genetics vs environment and intuition. In this movie, Louis Winthorpe, III played by Dan Akroyd snobbishly brags to Penelope after Billy Ray Valentine played by Eddie Murphy was arrested for allegedly stealing Louis’ briefcase…Louis: Someone has to take a stand against criminals. Penelope: But he could have killed you. Louis: In such a situation, you have no time to think - instinct takes over. It’s either kill or be killed. This is an example of pretentious intuition.

Surgeons, physicians, physician-extenders, nurses or anyone who must make snap decisions under crisis situations frequently apply intuition, gut-feeling or instinct to make snap decisions under crisis situations. None of us, especially our patients would want us to be frozen in indecisiveness during life-threatening situations, although at times doing nothing may be best.

We cannot ignore the wisdom of time, history, or our founders of the ISHLT, those who’ve been there, done that, lest we make the same mistakes. We cannot ignore all experiences which contribute to wisdom. It is important in our journey from raw intuition (novice) to refined intuition to access all information and others’ experiences. This will allow us to devise analytical modeling for implementing intuition which moves us to another plane of raw intuition, hopefully a higher plane, Figure 2. Repeating this cycle under ideal conditions by constantly questioning and testing our intuition, preconceived notions, with science again and again leads us to the wisdom of the aged. But beware of cognitive biases and ill-conceived notions. We probably spend more time in blind alleys than we care to admit.

We are all specialized experts in the ISHLT, therefore we have honed and will continue to hone our own abilities through constant discernment of many patterns: deleted, filtered, and matched, resulting in some level of intuition. Use your intuition. Use it with caution.

The ISHLT Links newsletter welcomes your ideas about the duality of art and science and the role of intuition in our endeavors, especially for our patients.
Since 2005, when the revised pathological classification for rejection first considered antibody-mediated rejection (AMR) in heart transplantation, the number of abstracts presented at ISHLT meetings on this topic increased about 6 fold, reaching a rate of 20% of the “clinical heart transplant” and “post heart transplant complications” and about 50% of the “pathology” abstract categories at the last San Diego meeting. Remarkably, at this meeting, one of the best-characterized experiences of AMR in lung transplantation was reported (A 85 from the Washington University in St. Louis). The high number of single-center reports was accompanied by two crowded pre-meeting symposia on AMR, and by Elizabeth Hammond’s Pioneer Lecture and career award for her landmark contribution to the pathological characterization of AMR in heart allografts.

The increase in reporting and space devoted to AMR testifies to the generalized interest of the transplant community towards this “new” entity in thoracic transplantation, but also highlights the knowledge gaps in diagnosis and treatment. Standardized recommendations based on multicentre studies are currently lacking.

The cardiac pathology working group reached a solid consensus on histological and immunohistochemical diagnostic criteria for AMR. The patterns of histological markers and capillary C4d/ C3d detection were defined, and coexistence of AMR and cellular rejection was recognized. The working group also provided high reproducibility of cross-readings, and diagnostic equivalence between immunohistochemistry and immunofluorescence techniques (see also June issue of JHLT). However, while the San Diego meeting clarified what is cardiac AMR from a pathological perspective, it did not provide comparable clarity for the clinical management and monitoring of cardiac AMR.

The largest number of abstracts on AMR and humoral immunity in general were presented by Salt Lake City and by Cedars-Sinai Groups, who differently stressed the importance of pathology vs. donor-specific antibodies detection. The main messages from these studies were: (1) either symptomatic or asymptomatic AMR bears a bad prognosis, (2) pre-transplant anti HLA antibodies increase the risk for post-transplant AMR (but not in all reports do they appear to affect survival), and (3) symptomatic AMR should be treated.

An additional important concept borne out of the meeting, also addressed in a paper by Nair in the June issue of the Journal (J Heart Lung Transplant 2011; 30: 612) is that AMR is an intricate process that develops through different stages (sub-clinical, accommodation, acute clinical, etc.) and requires several pieces of information to be diagnosed: pathology, immunohistochemistry, antibody detection, clinical examination and history, and graft function analysis. The intrinsic complexity of the phenomenon emphasizes that clinical management cannot be answered by single-center or retrospective studies and raises the following questions:

- Should we treat asymptomatic/sub-clinical AMR?
- What is the most efficacious and safe treatment for AMR (i.e. plasmapheresis vs. immunoabsorption vs. IVIG; ATG vs. rituximab vs. bortezomib)?
- How to monitor in the long term for AMR (biopsies beyond the first year vs. anti-HLA monitoring vs. customized approach)?

Moreover, organizational and economic issues have to be faced in everyday practice to set up a routine system that allows monitoring, diagnosis, decision making, logistics and treatment for AMR. This involves many more people and laboratories than a simple course of intravenous steroids in the outpatient department, after an afternoon call of the pathologist reading a H&E stain of a 2R (i.e. 3A) cardiac rejection.

ISHLT councils and boards, together with members’ continued input, will be pivotal in driving the transplant community to answer these questions. Given the low-likelihood of industry-driven studies forthcoming, the field is open (and needs linking…) to gather forces towards independent and multicenter studies/registries… while waiting for Prague 2012.
For the past 70 days since the 31st ISHLT meeting, we have been developing a structure for the LINKS e-newsletter. We know the importance of structure for anything to function: living entities, families, communities, cultures, governments, and organizations, especially the ISHLT and this e-newsletter. Without structure, there can be no function. Without function, there can be no refinements to structure.

Since becoming your editor for this newsletter, I have focused on creating structure. I hope I have assembled it properly in order for it to function appropriately, and to serve us well. I have had considerable help and guidance from Susie Newton. Many others have offered their assistance but only a few actually have given their support.

The June Issue focused on structure, mostly in the form of style. I shared with you a mission of harmony and understanding with examples of my stylish links. Whether these connections become useless or useful remains to be determined. We allowed you to peek in my windows to reinforce the importance of style and offered you the opportunity to share your style with the LINKS. Finally, as a move toward function, a few rules of engagement were offered. There was an emphasis on challenging the status quo. But more importantly, proposed “ground rules” are shaping up to improve us all. These rules will need constant refining.

For this July Issue, we have near completion of the structure. The structure comprises yours truly, Senior Associate Editors, Associate Editors, and an International Correspondents Board to ensure global representation. With these pieces in place, we will start working on function and refining the structure by either greasing or replacing the squeaky parts. You will notice a constant feature of the LINKS: “Quotable Quotes”.

For function, the essay on Intuition is my lame attempt to share with you on how we become less ignorant or experts. Well, it may be possible for some, but it seems impossible for me. The duality of art and science serves us well in medicine and surgery. There are many other dualities: day and night, good and evil, inside and outside, left and right, up and down, just to name of few. Again I am trying to compel all of you to share your ideas in the LINKS, vgvalent@utmb.edu or vvbones@gmail.com.

I would like to extend my thanks to all members and Councils for their hard work preparing, prioritizing and submitting symposium and plenary proposals for the Prague meeting. We received more than 130 proposals, by far eclipsing the number received in prior years. As the vast majority were fully detailed and well thought out, we have a wealth of material to build a program structure for Prague. Great work!

Stay tuned for an update in the August Links.
AZITHROMYCIN IN LUNG TRANSPLANTATION

Rajat Walia, MD

Chronic allograft dysfunction occurs in about 50% of patients and is the major factor limiting 5-year survival to about 50%. Following the success of erythromycin in diffuse panbronchiolitis, several groups examined the role of newer macrolides for preventing and treating the bronchiolitis obliterans syndrome (BOS). Few retrospective and prospective studies showed improvements in the FEV-1 clinically and statistically. In some reports, high BAL neutrophilia, typically greater than 15% were associated with a response to azithromycin. Two recent studies by the Belgian group studied this in greater detail. The first study published in the Journal of Heart and Lung Transplantation, December 2010 retrospectively looked at long-term azithromycin therapy for BOS in 103 patients and showed an improvement in pulmonary function and survival. The second study by the same group published in the European Respiratory Journal, December 2010 was a randomized, prospective, placebo-controlled trial looking at the role of azithromycin in preventing BOS and showed a much lower incidence of BOS in patients treated with azithromycin. One should note, these studies are from the same institution and that while other confounding factors should be considered, such as an effect on gastric motility and the potential treatment of difficult to diagnose organisms such as *Chlamydophila* spp, the addition of azithromycin is the first intervention that appears to alter the natural history of lung function decline in patients with BOS. In a separate long-term study, clarithromycin had no effect on BOS or survival. Although clarithromycin is a different macrolide, a multicenter, randomized controlled study is necessary before azithromycin can be considered a standard in the prevention and treatment of BOS.

References:
**FOOD FOR THOUGHT**
**The Infectious Diseases Council**

The recent outbreak of enterohemorrhagic E. coli (EHEC) from Germany has had deadly consequences across Europe, with effects reaching the U.S. and Canada. In its wake are well over 3,000 sickened patients with a 13% mortality rate. While this episode is subsiding, it brings to mind the importance of safe living for our vulnerable and immunosuppressed cardiothoracic transplant recipients.

Economic and logistical problems stymie our public health institutions’ ability to prevent all food-borne infectious outbreaks. Coupled with the ever-growing internationalization of food supplies, we as transplant physicians and caregivers must take responsibility at the individual level and appropriately educate our patients on the importance of food safety. Here are just a few highlights to remind our patients:

1. **Hand hygiene** is a constant priority. Hands should be washed before preparing food and before eating, after touching plants or soil, and after cleaning up after pets or coming in contact with animals.
2. **Avoid** drinking or eating foods with unpasteurized milk or dairy and unpasteurized fruit or vegetables.
3. **Do not** eat raw or undercooked eggs, meat, seafood, or poultry.
4. **Do not** eat raw sprouts.
5. **Avoid** cross-contamination when preparing foods at home (use cleaned or separate cutting boards, utensils, etc. for raw meats and vegetables).
6. **When traveling**, transplant recipients should not eat raw, unpeeled fruits or vegetables.

Unfortunately, controlled studies of these measures do not exist in transplant populations, and our knowledge of food-borne gastroenteritis in transplantation is limited to case reports and historical case series. Therefore, intuition and good home-cooked sense or reason will go a long way. Although strict adherence to these sensible and reasonable measures may not eliminate all risks, they will prevent many potential problems. A moment in time to remind one patient of the importance of something as simple as washing their hands may lead to a lifetime of good health. Bon appétit and be safe!

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**ISHLT ADMINISTRIVIA**

- The International Society for Heart and Lung Transplantation has embarked on a [History Project](http://www.ishlt.org/historyandArchives/videoInterviews.asp) to collect reminiscences and thoughts from leaders and pioneers in the field of heart transplantation to enrich the educational content of the Society. The project began in April 2009 in Paris, France, with video interviews of some of these important leaders and continued in April 2010 and 2011 with more video interviews. Individuals whose interviews have been captured to date include: Leonard L Bailey, MD, William A Baumgartner, MD, Joel D Cooper, MD, Christian Cabrol, MD, Jack G Copeland, MD, Sir Terence English, KBE, FRCS, O Howard Frazier, MD, Elizabeth Hammond, MD, Michael L Hess, MD, Roland Hetzer, MD, PhD, Sharon A Hunt, MD, Stuart W Jamieson, MB, FRCS, James K Kirklin, MD, Robert L Kormos, MD, Alan H Menkus, MD, FRCS(C), Leslie W Miller, MD, John B O’Connell, MD, Bruno Reichart, MD, Bruce A Reitz, MD, Eric A Rose, MD, John Wallwork, FRCS, and Lori J West, MD, DPhil. Please visit [http://www.ishlt.org/historyandArchives/videoInterviews.asp](http://www.ishlt.org/historyandArchives/videoInterviews.asp) to view these wonderful, engaging conversations.

- ISHLT is pleased to announce a new initiative under the Grants and Awards program: the [International Travelling Scholarship Award](http://www.ishlt.org/historyandArchives/videoInterviews.asp). The purpose of this award is to facilitate the exchange of knowledge and techniques regarding heart and lung transplantation and the treatment of end stage heart and lung failure and to build relationships between individuals, institutions, and countries. The Scholarships may be used to learn new techniques in the clinic, operating room, or laboratory or just to experience first-hand how others deal with challenging problems. Each award will be in an amount of up to $6,000, and ISHLT will fund a minimum of ten Travelling Scholarships annually. All members of the Society are eligible to apply for a Scholarship. It is anticipated that each Scholarship will be for up to
“ISHLT ADMINISTRIVIA” continued

Above all, brief and to the point undermine all rules. During oral presentations, we should stay within our allotted time out of respect for other presenters and our audience. Any creative idea as long as it is pertinent to the ISHLT is welcomed for publication in the LINKS. Rules are made to be broken. (Remember Prague, not the Alamo). This is a summary of the first set of rules from the June Issue for the ISHLT.

To underscore these important “golden” rules, think of the following when giving your next oral presentation. Wouldn’t it be simpler to say “now” instead of “at this particular point in time?” I have been guilty of this, and this seems to be a near ubiquitous problem for all speakers. How about when a speaker is pointing to a figure or a table on his/her slide and says, “as you can see here” or “this figure shows.” The audience can see and know if it is a figure or table. What the audience wants is your explanation of the results. And if it is one row of data you point to, why clutter the slide with other rows? Then, don’t you want to just take off a shoe and throw it (December 2008, Baghdad Press Conference) or a banana (June 2011, World Cup) at the clown behind the lectern when a presenter states, “I know you can’t read this slide but…” or “I know the print is small, but please “bear” with me…” In such instances, we should stop the presenter and ask him or her to go ahead and “bare” first. In addition, what about the proverbial “messy” slide? Finally, be careful of the lengthy introductions during mini-oral presentations. Get to the point. It’s not just the presenter, but often it’s the senior author or mentor who is guiltier of encroaching on the allotted time and diluting the point. There are all kinds of rules about slides with which few people comply. Remember the golden rules!

For the newsletter, associate editors are expected to provide at least two summary articles a year and show evidence of: 1/ actively assisting in soliciting writers, 2/ generating ideas or 3/ challenging or criticizing any concepts presented in meetings, publications, the LINKS, or elsewhere. Members of the International Correspondents Board must submit one article or solicit at least one that is accepted for publication per year. Therefore, the associate editors and members of the International Correspondents Board have a year to prove themselves worthy.

As suggested in the June issue the vision of the LINKS is to keep members abreast of current events, provide snippets of informative pieces gleaned from meetings, publications and conversations, and sprinkle in entertaining, amusing and humorous (not humerus) links from our world of knowledge, pertinent to the ISHLT. It should be a means for any member to express their opinion, counter a point previously brought up, or whatever is on their mind. Feel free to throw us a bone. I might fetch it.

• Reminder – the deadline for submitting applications for the Branislav Radovancevic Memorial Fellowship Award is July 15, 2011. For more information about this award, please visit http://www.ishlt.org/awards/radovancevicMemorial.asp.
NHSAH council is looking for all interested members to join! Did you know that ISHLT members can join as many Councils as they like? All nurses, social workers, pharmacists, therapists, psychologists (basically anyone who has not been to medical school though docs are welcome, too!) is encouraged to join our council by checking the box on their ISHLT member profile. Visit the ISHLT Members Only Website to update your profile page. Up to 36 Continuing Education Points for Transplant Certification (CEPTC) were awarded to 45 attendees of the 31st Annual Meeting and Scientific Sessions (April 13-16, 2011 San Diego, California). This is more than half the credits required for renewal of ABTC certification every five years! If you are an ABTC certified nurse who attended the meeting in April and would like your CEPTCs, please contact Phyllis Glenn in the ISHLT Headquarters office (Phyllis.glenn@ishlt.org).

Do you have an idea about how NHSAH can better meet your clinical, research or professional development needs? We want to hear from you! Please reach out to any of the members of the NHSAH leadership council (http://www.ishlt.org/councils/nursing.asp). Better still, consider making a contribution to the council. The NHSAH Development Task force is keen for new members and this is a great way to get involved. If you are interested, please contact Arzellra Walters (arzellra.walters@mountsinai.org).