VINCENT’S TWO SENSE:

The Ides of March, the Luck of the Irish and the Vernal Equinox are fast approaching. In this issue, there are articles from the Pathology and Pulmonary Hypertension Councils. Included, we have messages from the International front and various announcements from our President, and congratulations to the winners of the Links Travel Awards. There are other important ideas contained within this special issue that might just give you pause to think and do what’s right for humanity’s sake. Read on.

PRE-REGISTRATION DEADLINE:

If you are planning to attend the ISHLT 37th Annual Meeting and Scientific Sessions, or one of the 2017 Academies, please keep in mind that the deadline to pre-register is Friday, March 17, at 11:59 PM EDT. Registrations received/postmarked after March 17 will not be processed and such registrants must go to Onsite Registration to register for the meeting. Higher onsite registration fees will apply. Fees for onsite Annual Meeting registration will be $300.00 more than the early bird fees, and fees for onsite Academy registration will be $100.00 more than the early bird fees. Avoid long lines and additional costs by registering NOW.

Register for the Meeting
Annual Meeting Website
IN THE SPOTLIGHT: 2017 Recipients of the ISHLT Leach-Abramson-Imhoff Links Travel Awards

Over the past year, the ISHLT again had a productive year from over 100 writers contributing to the ISHLT Links Newsletter. To deter us from analysis paralysis, we must decide, sometimes with “Big Decisions” but not always the right decision. From power dynamics and groupthink to group polarization, our decisions are subjected to biases resulting in decisions that could be hazardous to someone’s life. A grid and a checklist will foster collaborative decision making to reduce hazards as we have decided on this year’s Links’ Writers of the Year. Congratulations from such big decisions and with what were you doing in 1996 to Pediatric Cardiac Prehab. Of course, the forever important and necessary discussions of difficult news with our pediatric transplant recipients shed light on our sensibilities about caring and compassion. In the end, simply showing up proves that it is all worthwhile. Here, our Writer of the Year Award goes to none other than Quincy Young. Our First Runner-Up is Monica Horn, and Honorable Mention awards go to Melissa Cousino and Erin Wells.

Let’s extend a warm ISHLT congratulations to these writers.

**Writer of the Year: $1,500**

Quincy Young, PhD, RPsych
St. Paul’s Hospital
Vancouver, BC, Canada
Qyoung@providencehealth.bc.ca

January 2016, Big Decisions

**First Runner-Ups: $1,000**

Monica Horn, RN
Children’s Hospital
Los Angeles, CA, USA
Mhorn@chla.usc.edu

January 2016, Pediatric Cardiac "Prehab"
October 2016, What Were You Doing in 1996

**Honorable Mention (2 recipients): $500**

Melissa Cousino, PhD
October 2016, "I didn't know this could happen:" Discussing Difficult News with Pediatric Transplant Patients

Erin Wells, RN, BSN, CPN
Northwestern Memorial Hospital
Chicago, IL, USA
Erin.Wells@nm.org

October 2016, Showing Up

Erin deserves a special congratulation on her three-peat honorable mention award.

History of the Leach-Abramson-Imhoff Links Travel Awards

The ISHLT Leach-Abramson-Imhoff Links Travel Awards, funded in part by the generous support from W.O. and Joan Leach (Gadsden, Alabama, USA), Mrs. Sue Abramson (Birmingham, Alabama, USA) and Mr. Larry Imhoff (La Place, Louisiana, USA), were created to support the growth and development of our future leaders from within our society including physicians, nurses, and other health care professionals. Those motivated enough with investigation, communication, and dissemination of new ideas for the betterment of patients with failing lungs and/or a failing heart including such conditions as pulmonary fibrosis, cystic fibrosis, emphysema, pulmonary hypertension, and from ischemic, nonischemic to congenital heart diseases should be awarded for their efforts.

Eligibility requirements include:

1. Any healthcare professional including but not limited to nurses, nurse coordinators, social workers, pharmacists, therapists, dietitians and early career physicians are eligible and must be a member of the ISHLT regardless of duration in their career.
2. An imposed restriction on physicians is that they must be in their Early Career—within 7 years of training, Assistant Professor equivalent, or junior faculty level with rare exceptions.
3. Individuals must display some form of research interest, basic, clinical, translational or outcomes investigations or at a minimum display some skill in journalism best exemplified by their contributions to the Links Newsletter engendering fresh and creative ideas.

Each year, the winners are selected from a pool of nominees by the ISHLT Links Travel Award Committee (LTAC). This committee includes the following individuals: the Links Editor-in-Chief, ISHLT Executive Director, ISHLT President, ISHLT Program Chair, and the Links Managing Editor.
A Message from Your ISHLT President

Dear ISHLT Members,

In these uncertain times, it seems vitally important for the International Society for Heart and Lung Transplantation to reaffirm our commitment to inclusivity and engagement of the global community involved in the care of patients with advanced heart and lung disease. A foundational principle of our Society has been to support our membership through scientific exchange, advocacy, and education. This charge was underscored in the recently developed ISHLT strategic framework in which one of our strategic imperatives is to “Engage Our Community Worldwide”. The ISHLT is a vibrant and healthy professional society enriched by our diversity. On behalf of the ISHLT Board of Directors, I strongly urge the entire membership to recommit to our global mission. Our patients and our disciplines deserve no less.

Sincerely,

Maryl R. Johnson, MD
Update from the Pathology Council

Brandon T. Larsen, MD, PhD
Mayo Clinic Arizona
Scottsdale, AZ, USA
Larsen.Brandon@mayo.edu

The Pathology Council is an active and exciting group that continues to provide vital, clinical research and educational expertise to advance the Society’s initiatives, strengthen the transplantation community, and most importantly, help the patients we serve! Antibody-mediated rejection (AMR) continues to be a strong focus of our Council’s efforts as we seek to better understand the phenomenon of AMR in cardiac and pulmonary allografts, refine our diagnostic criteria and relevant biomarkers for such, and disseminate this information to pathologists. To this end, the Council put together several collaborative research groups over the last year to facilitate multi-center studies on these topics, and our members continue to expand available online resources for transplant pathology.

Pathology Council Initiatives

Over the last year, the Council has established several working groups to investigate various aspects of AMR. Gerry Berry together with Ornella Leone, Annalisa Angelini, Patrick Bruneval, and Jean Paul Duong Van Huyen are forging ahead with a project investigating inflammatory burden in cardiac AMR in collaboration with other institutions, and this project is ongoing. Second, the Council has increased its efforts to investigate potential markers of chronic rejection in biopsies, learning from experiences gained in other solid organ transplants. Martin Goddard, Elizabeth Hammond, Bobby Padera, and Annalisa Angelini are moving forward with research efforts on this topic in collaboration with other institutions. An excellent summary of the unanswered pathology questions in cardiac AMR was published in January by Patrick Bruneval and colleagues in AJT, and is an excellent read for those wishing to see where we are going from here (https://www.ncbi.nlm.nih.gov/pubmed/27862968).

For those of you who missed it, Dr. Levine and colleagues in the ISHLT Pulmonary AMR Working Group (including several members of our Council) published a much-needed and long-awaited consensus definition for pulmonary AMR a few months ago, including degrees of diagnostic certainty and incorporating clinical, serologic, and histologic features into the definition (https://www.ncbi.nlm.nih.gov/pubmed/27044531). This publication also includes a very useful online supplement that outlines current research priorities, many of which are being actively investigated by members of our Council. Hopefully these problems will also prompt you to join the effort! Stay tuned for updates, and we look forward to seeing many of you at the Annual Meeting next month so we can coordinate these efforts and push forward.

Members of the Pathology Council also continue to be engaged in concerted efforts to develop better online tools for transplant pathology. In recent years, members of our Council have developed an online tutorial, including online quiz components, on cardiac ACR and AMR for
pathologists in partnership with the Society for Cardiovascular Pathology and Association for European Cardiovascular Pathology (http://scvp.net/acr/index.html). Pulmonary pathologists have also begun to develop online tools to aid pathologists in interpretation of lung transplant biopsies. In the last year, our European colleagues led by Fiorella Calabrese have developed a tutorial website for pulmonary AMR, hosted by the European Society of Pathology (http://lungtransplant.dctv.unipd.it/amr/index.php). This website is a work in progress. If you encounter good examples of diagnostic grades of rejection or other entities in lung transplant pathology that could be included in this online resource, please contact Fiorella Calabrese at fiorella.calabresse@unipd.it. Both of these online resources continue to be well received, but suggestions for improvement are welcome.

The Pathology Council remains small compared to other Councils in the ISHLT, and this has unfortunately not changed very much in recent years. Most pathologists who evaluate heart and lung transplant biopsies are not ISHLT members and do so as a small component of their broader practices. The ISHLT Board is keen that we continue to engage with our pathology colleagues, including those who are non-members. We urge our Council members to continue reaching out to pathologists in other centers who practice transplant pathology, to keep them informed and to encourage them to consider joining us. There is considerable expertise in transplant pathology out there among non-members that remains untapped! Please bang the drum and spread the word.

2017 Annual Meeting & Scientific Sessions in San Diego, CA.

Perhaps the most important news related to the upcoming Annual Meeting in 2017 for busy pathologists is a change in the format of the Annual Meeting. Beginning with this meeting, program content relevant to the Pathology Council will be clustered into a single day (Friday, April 7), instead of being distributed throughout the entire meeting over several days. Hopefully this concentration of program content will shorten the time away from our practices and allow more of our members to attend. Please spread the news to your pathology colleagues, especially the ones who may have been interested in the past but couldn’t attend due to time constraints. In any case, you don’t want to miss our exciting pathology-oriented sessions in San Diego next month.

For more details about the upcoming Annual Meeting and the official program of scheduled events, please check the ISHLT website at http://www.ishlt.org/meetings/annualMeeting.asp.

See you in San Diego!

Disclosure statement: The author has no conflicts of interest to disclose.
There's no RV in ReVerse...or is there?

Jeremy A. Mazurek, MD
University of Pennsylvania
Philadelphia, PA, USA
Jeremy.Mazurek@uphs.upenn.edu

While there is an extensive literature dedicated to left ventricular (LV) reverse remodeling in heart failure (HF), with current staples of HF therapy proven to not only improve outcomes but also improve left heart structure and function, the same may not be true for the right ventricle (RV) in pulmonary arterial hypertension (PAH). A simple ‘pubmed’ search using the terms “LV reverse remodeling” produced 785 results, while a search of “RV reverse remodeling pulmonary hypertension” yielded only 52 items. So the question remains: In PAH, does the RV reverse remodel after the initiation of pulmonary hypertension (PH)-specific therapy?

PAH is a rare condition characterized by significant elevations in pulmonary artery pressure and pulmonary vascular resistance that results in high RV afterload leading to exercise intolerance, RV failure and ultimately, death. It is the RV adaptation to this increased load, and not pulmonary artery pressure elevation per se, that dictates clinical symptoms and outcomes.

Initial RV hypertrophy gives way to progressive RV remodeling and maladaptation, perpetuated by RV ischemia and a glycolytic shift in RV metabolism, eventually leading to RV failure [1]. Thus, despite advances in PAH therapy over the last 2 decades, largely directed at the underlying pathobiology at the level of the pulmonary vasculature, morbidity and mortality remain quite high. And while prior study has shown dramatic improvements in RV structure and function in the subset of patients with PAH who have undergone bilateral lung transplantation, and in those with chronic thromboembolic PH who have undergone successful pulmonary thromboendarterectomy, the majority of patients with PAH are often on long-term, double and triple drug combination PH-therapy, whose effects on RV reverse remodeling are less definitive [2].

Data from the early days of sildenafil and bosentan show a reduction in RV mass, and improvements in RV:LV ratio and eccentricity index when sildenafil is added to bosentan therapy as compared to bosentan alone [3-5] This is matched by improvements in hemodynamic metrics including PVR and cardiac index (CI), as well as improvements in NT-proBNP levels. Interestingly, long-term epoprostenol therapy was not found to reverse RV dilatation and hypertrophy [6]. Study of the effects of newer PH therapies on RV reverse remodeling is currently underway [7, 8].

As the effects of modern PH therapies on hemodynamic and imaging parameters of RV structure and function are further clarified, we are able to better risk stratify patients not simply based on baseline values, but rather on improvement in values or absolute values on serial assessment after exposure to PH-specific therapy. Nickel et al. found that while many traditional parameters were predictive of survival at baseline (including WHO functional class, CI, mixed-venous O2 saturation, and NT-proBNP), follow-up assessment of these parameters in response to therapy were more predictive of prognosis than baseline values [9] Similarly, serial RV ejection fraction (RVEF) in
response to PH-specific therapy was superior to baseline RVEF in assessing patient outcome in PAH with a survival advantage of a follow-up RVEF > 35% vs. < 35%, independent of change in PVR [5, 10].

Recently, we reported on the prognostic value of follow-up tricuspid annular plane systolic excursion (TAPSE), an easily assessable and reproducible echocardiographic metric of RV function, in a PAH population [11]. Previous reports showed the prognostic significance of baseline TAPSE in a PAH population with a nearly 4-fold increased risk of death in patients with reduced baseline TAPSE. That study, however, assessed TAPSE at one undefined time-point, and thus, it did not reflect the prognostic value of echo-derived RV function in response to PH-specific therapy [12].

In the recent report, we evaluated 70 patients with PAH with baseline and follow-up echocardiography after the initiation of PH therapy. We assessed the prognostic role of follow-up TAPSE and specifically a treatment TAPSE goal of ≥ 2cm, which is reflective of normal RV function. Overall, 66% of patients were on double or triple combination therapy at follow-up (median time to follow-up echocardiogram was 384 (201-753) days) with a significant improvement in TAPSE (1.6±0.5 cm vs. 2.0±0.4 cm; p< 0.0001), along with improvements in other echocardiographic and functional parameters at follow-up. Importantly, while baseline TAPSE stratified at 2 cm did not predict survival in this cohort, when we stratified by follow-up TAPSE ≥ 2cm there was a significant survival advantage in those with follow-up TAPSE ≥ 2cm as compared to those with follow-up TAPSE < 2 cm (log-rank p=0.004; HR 0.21, (95% CI 0.08-0.60)).

Furthermore, 28 of 37 patients (76%) with follow-up TAPSE ≥ 2cm had a TAPSE < 2 cm at baseline, with 19 of 37 (51%) having a baseline TAPSE ≤ 1.6 cm. This group, therefore, was representative of patients with significantly reduced TAPSE at baseline that improved to normal at follow-up after initiation of PH-specific therapy. Thus, we propose that follow-up TAPSE ≥ 2cm is both an achievable treatment target, as well as a powerful prognostic marker in patients with PAH.

This data supports the call from the 5th World Symposium on PH for “the need to identify clinically relevant treatment goals that correlate with long-term outcome” [13]. It also highlights the role of echocardiography, which is noninvasive, relatively inexpensive and widely available in identifying the ability of the RV to indeed ReVerse remodel in the setting of PH-specific therapy. Further work in this area is needed with the development of more therapies, and specifically RV-targeted therapies, to ultimately provide even better outcomes for our patients stricken with this condition.

Disclosure statement: The author has no conflicts of interest to disclose.

References:
Hiding in Plain Sight: Harvest of Pulmonary Artery Endothelial Cells from Discarded Swan-Ganz Catheter Balloons May Illuminate PAH-Specific Biological Processes

Michael J. Passineau, PhD
Allegheny Health Network
Pittsburgh, PA, USA
Michael.Passineau@ahn.org

The diagnosis of pulmonary hypertension (PH) requires right heart catheterization (RHC), thus this diagnostic procedure becomes the gateway through which patients enter into management of PH, regardless of the etiology. While the hemodynamic information obtained by RHC is crucial to the management of PH, hemodynamics alone provide relatively little insight into the biological processes underlying pulmonary pressure changes, and thus a constellation of additional clinical observations are needed in order to properly assign a patient to the appropriate WHO Group classification.

In 2013, we reported in the *Journal of Heart and Lung Transplantation* that it was possible to recover Pulmonary Artery Endothelial Cells (PAECs) from the balloon tips of Swan-Ganz catheters after RHC. Our initial thoughts, which were shared by interested collaborators, were that culturing and expanding these cells would provide a new resource for determining patient-specific treatments, and possibly help to elucidate pathologic disease mechanisms, particularly in WHO Group I disease. The downside of this culture approach however, was twofold. First, it took several weeks to establish robust cultures, making it difficult to use these cells for diagnostic applications. Second, cultures probably favor a subset of harvested cells, possibly endothelial progenitor cells, that manifest a superior ability to survive and proliferate in culture. Thus, PAEC cultures probably do not reflect the *in situ* situation in the pulmonary artery with full fidelity.

To expand the versatility of this technique, we modified our protocol for harvest in order to perform direct analysis of PAECs without the need for an intermediate culture step. Several years of work have resulted in a reliable process that utilizes anti-CD45 affinity columns for leukocyte depletion followed by anti-CD146 columns for positive selection of PAECs yielding harvest that typically number in the 5000-20,000 live PAECs for downstream analysis. Importantly, we have shown that this process can be applied to catheter tips shipped overnight on wet ice, with cell viability remaining above 25% and overall numbers in the thousands of PAECs. This “clip and ship” protocol has become standard practice in our research group and we welcome receipt of catheter tips from centers throughout North America for collaborative projects.

Our interest has focused intently on biological markers potentially useful for differentiating WHO Group I pulmonary arterial hypertension (PAH), particularly its idiopathic form, from occult left-sided heart disease. Some patients with left heart failure with preserved ejection fraction (HFpEF) and those with combined pre and post capillary pulmonary hypertension (CPCPH) can present a vexing clinical entity which can be difficult to differentiate from PAH. Hemodynamic maneuvers,
such as fluid or exercise challenges can be particularly useful in these instances, but are not completely reliable. Because the biology of PAH seems to have a unique disease process, we turned to earlier literature wherein histopathological and molecular studies of explanted lungs from PAH patients hinted at a role for bcl-2 in driving anti-apoptotic activity in PAECs [1-3]. Intriguingly, we have now been able to report single-center, unblinded data associating a flow cytometry-based index of bcl-2 in harvested PAECs with Group I PAH to the exclusion of HFpEF [4]. More work will be needed to confirm these findings with the current emphasis on obtaining a double-blind study carried out at multiple expert PAH centers. If independently validated, this new approach has great potential for increasing the precision of WHO Group I diagnosis.

Looking forward, it is important to remember that the regions of the pulmonary artery contacted by the Swan-Ganz catheter balloon are very proximal to the right ventricle. Yet, the pathophysiology of PAH, particularly the manifestations of anti-apoptotic phenotypes, presumably begins in the distal microvasculature, very remote from where a Swan-Ganz catheter would ever venture. So how do we reconcile the findings of Benza et al [4] from the standpoint of this presumed proximal/distal disconnect? Could the molecular pathophysiology of the distal vasculature in PAH be propagated distally to PAECs of the secondary and tertiary branches of the Pulmonary Artery? As implausible as this sounds, our observations suggest it may indeed be the case.

If so, what else could be learned about the distal microvasculature of a PAH patient from a Swan-Ganz catheter that would otherwise be discarded after RHC? Moreover, could it be that the emergence of an anti-apoptotic phenotype in the pulmonary vasculature heralds a disease process that is specifically responsive to PAH-specific medications? In complex disease, or so-called out-of-proportion PH, what will we observe with respect to this biological mechanism, and will it unlock a new approach to improved treatment outcomes by serving as a triggerpoint for deployment of PAH specific therapy?

These questions and more present an exciting new frontier for a more nuanced understanding of PAH pathophysiology, and possibly that of HFpEF as well. The past two decades have seen remarkable progress in PAH treatment. Indeed, it is worth reflecting on how the advent of not one, but four different classes of PAH-specific pharmacotherapies have transformed a grim, inevitably fatal prognosis into a serious condition in which a subset of patients respond and survive remarkably well. The advent of this technique, amounting to in essence a cellular biopsy of the pulmonary endothelium in situ, compels us to hone more precise treatment algorithms to use these powerful pharmacotherapies in biologically-targeted, patient-specific strategies.

The irony for the PAH physicians is that clinicians performing RHC have for decades been discarding Swan-Ganz catheters on which thousands of their patients’ own PAECs have been hiding in plain sight. Sometimes the most exciting advancements are remarkably simple. Time will tell what the PAH community will make of this new frontier!

Disclosure statement: The author has no conflicts of interest to disclose.
References:


Pathologic Lesions of Chronic Thromboembolic Pulmonary Hypertension

Belinda Rivera-Lebron, MD, MS
Riveralebronbn@upmc.edu

Michael G. Risbano, MD, MA
Risbanomg@upmc.edu
University of Pittsburgh
Pittsburgh, PA, USA

Acute venous thromboembolism resolves in most cases. However, an estimated 0.5%-3.8% of pulmonary embolism (PE) survivors develop chronic thromboembolic pulmonary hypertension (CTEPH) resulting from mechanical obstruction of the pulmonary arteries [1-3]. Most patients with CTEPH have experienced a PE in their lifetime; however, up to 25% of patients have never reported a thrombotic event [4]. Patients may present with exertional dyspnea, fatigue, palpitations, lightheadedness or syncope. CTEPH is diagnosed by precapillary pulmonary hypertension (mean pulmonary arterial pressure > 25 mm Hg and pulmonary arterial wedge pressure ≤ 15 mm Hg) on right heart catheterization and abnormal ventilation perfusion scintigraphy (VQ scan) including at least one mismatched perfusion defect with confirmatory imaging by either computed tomography (CT) angiography or pulmonary angiography [5].

CTEPH is primarily caused by the transformation of incomplete resolution of thrombi into fibrotic organized fibrotic scar tissue. Residues of organized thromboembolic material can be found in large pulmonary arteries, frequently called “webs,” can adhere to the arterial wall, and are composed of collagen, fibroblasts and inflammatory cells [6]. Neovascularization then follows, presumably as the effect of clot organization. Inflammatory markers, such as IL-8, VEGF and basic fibroblastic growth factor, stimulate angiogenesis and facilitate thrombus resolution [7].

Pathologic examination of lung biopsy, or an autopsy of patients with CTEPH, disclose the full range of pulmonary hypertensive lesions in the small pulmonary arteries [8]. Muscle hypertrophy of the arteries and arterioles and medial thickness is the most common finding, but eccentric intimal fibrosis, concentric laminar intimal fibroelastosis and internal fibromuscular proliferation is also seen. Organized thrombi is present in small pulmonary arteries. Plexiform lesions, the typical histological hallmark of idiopathic pulmonary arterial hypertension (IPAH), is described by one group [8], but not seen by another group [9]. These histopathologic findings are very similar to those seen in patients with IPAH, making it challenging to pathologically discriminate between the two groups of patients.

Impaired fibrinolysis and altered fibrinogen structure and function may also be implicated in the failure of thrombus resolution [7]. Inherited thrombophilia and anti-phospholipid antibodies have been found in 17% and 10% of CTEPH patients, respectively [7]. However, the frequency of protein S or C deficiency, factor V Leiden mutation and the prothrombin 2021G mutation have not consistently been found to be more common in CTEPH than in the general population [3].
Pulmonary hypertension develops once a threshold level of pulmonary vascular obstruction is reached, and right ventricular changes are seen when over half of the effective pulmonary vascular bed is affected [6]. Interestingly, studies have demonstrated a poor correlation between the degree of vascular occlusion by thrombi and the severity of hemodynamic compromise, which suggest additional processes contributing to the development of CTEPH [3].

Despite the advances in the last years, we still don’t fully understand the cause of thrombus non-resolution, which for most is considered the initial trigger for CTEPH pathogenesis. It is not known whether the development of CTEPH is related to the extent and location of the thrombi, or due to a genetic predisposition or if the use of thrombolysis reduces its incidence. Further research in these complex areas will advance the early diagnosis and expand treatment options of patients with CTEPH.

Disclosure statement: Dr. Rivera-Lebron receives consulting fees from Gilead and serves as site PI for a clinical trial from Actelion. Dr. Risbano has received consulting fees from Gilead and Actelion and serves as the site PI for clinical trials from Actelion and United Therapeutics; he is the recipient of a grant from Gilead for an investigator sponsored research project.

References:
Pulmonary Arterial Hypertension, 25, and the Holy Grail

Timothy Baillie, BBiomedSC, BMBS, FRACP
Toronto General Hospital
Toronto, ON, Canada

Arbitrary: based on random choice or personal whim, rather than any reason or system.

Undertaking a Fellowship should provide an opportunity to think and to ask questions. Moving to Toronto from Australia some months ago to continue training in my area of interest, pulmonary hypertension, I have been thinking: why is the sun so far away? Why aren’t there more venomous creatures around? Why is Pulmonary Arterial Hypertension (PAH) only recognized as a ‘problem’ once hypertension arises, when it was noted that Primary Pulmonary Hypertension (now PAH) was best described as a "plexogenic pulmonary arteriopathy" back when gasoline (AKA Petrol) was 44c a gallon (AKA 3.785 litres) and you could pick up a new and improved version of the Ford Mustang (AKA Ford Mustang II) for $4105 (all USD of course) {Hatano S, 1975 #1273}? If PAH is a pulmonary arteriopathy, why is a mean pulmonary arterial pressure (mPAP) of 25mmHg a prerequisite for diagnosis? How did 25 come about and what is wrong with, for instance, 24mmHg? Did a youthful Harrison Ford (HF) put himself through all that in search of a metallic drinking vessel, or was it an appetizer for the blockbuster "Indiana Jones and the Last Last Crusade," where a mature HF successfully navigates the bureaucratic minefield of medical research to realize the true Holy Grail, pre-clinical detection of PAH?

Before we address these questions, we need some background. Pulmonary hypertension (PH) is defined by an elevated resting mPAP (25mmHg) measured by right heart catheter (RHC). Pathophysiological conditions causing PH are pigeonholed into one of five categories based on common clinical, pathological and hemodynamic findings, and similar treatment strategies {Galie, 2016 #1068}. Pulmonary arterial hypertension represents Group 1 PH, and includes idiopathic and heritable PAH, PAH associated with underlying connective tissue diseases (CTD), such as systemic sclerosis and systemic lupus erythematosus, HIV, porto-pulmonary hypertension in the setting of liver cirrhosis, congenital heart disease and drug or toxin induced PAH. Idiopathic and CTD-associated PAH makeup much of the estimated 15-60 prevalent cases per million population {Peacock, 2007 #539}. Complex and incompletely understood metabolic, molecular, structural and functional changes drive the disease process, resulting in vasoconstriction, arterial wall remodeling and in situ thrombosis (histologically described as ‘plexiform’ lesions) which ‘obliterate’ small pulmonary arterioles. As the “plexogenic pulmonary arteriopathy” progresses, resistance to blood flow through the pulmonary vasculature rises, elevating pressures and placing undue strain on the right ventricle (RV) which, unchecked, results in RV failure and reduced life expectancy despite effective but non-curative medical therapies.

Now back to the questions. To knock the easy ones off, I have been told by unreliable sources that the faraway sun long ago drove nearly all venomous creatures to warmer continents – thank you on behalf of my fellow Australians. What is more ambiguous is the importance of a mPAP of 25mmHg in PAH. Different - but equally unreliable - sources have informed me this magical
number was conjured in an idyllic chalet in the Swiss Alps by a small group of well-informed scientists enjoying delicate Trappist Ales [Note: I could not confirm this despite extensive PubMed searching]. The reality is that deranged hemodynamics at rest are a late consequence of the underlying pulmonary vascular disease. In fact, a majority (50-60%) of the pulmonary microcirculation are lost by the time the mPAP rises ≥ 25mmHg {Lau, 2011 #427} and close to a 40% deficit can be absorbed by one’s reserve without any impact on their resting mPAP (upper limit normal being ~19mmHg {Kovacs, 2009 #533}). Why, therefore, do we define a disease that is first and foremost a pulmonary vasculopathy by arbitrary hemodynamic abnormalities that occur late in the disease process, particularly given certain populations at risk of developing the disease (e.g. systemic sclerosis) are readily identifiable and treatment is known to be most effective when instigated early {Lau, 2014 #956}? The unifying answer: the ‘hypertension’ component of PAH is readily measured whereas ‘early disease’ (vasculopathy without hemodynamic derangement) is not. Yet.

I had intentions of discussing some of the exciting progress being made by researchers around the globe in the search for the Holy Grail. Unfortunately, I used up my word count discussing animals and weather, and am also practicing the art of creating ‘dramatic suspense’ in the expectation I will be contracted by Lucasfilm soon. I will say that progress is being made via different approaches including standardized exercise protocols (observing for abnormal hemodynamic responses using invasive and non-invasive techniques), standardized magnetic resonance imaging protocols utilizing intravenous adenosine to detect reduced cardiopulmonary reserve, functional nuclear imaging to assess postural changes in lung perfusion, and metabolomics, whereby a certain ‘metabolic signature’ may suggest impending PAH. I should also note that this is not an easy research topic, largely due to the absence of a validated method against which results can be compared. Consequently, researchers necessarily extrapolate differences observed between healthy and PAH subjects, that is they assume that subjects with early disease will fit “somewhere in the middle.” Only long-term trials with the capacity to quantify incident PAH cases will be definitive.

In summary, PAH is a late result of the underlying pulmonary vasculopathy with a mPAP of 25mmHg, reflecting an arbitrary ‘line in the sand’ that once crossed, simply confirms that the pulmonary vascular disease has progressed to a point that is readily measured. A paradigm shift towards early detection of this disease is possible in certain populations, but like HF, researchers will have to navigate a number of obstacles in order to realize their quest for the Holy Grail, although I am confident a similar ending will transpire.

Disclosure statement: The author has no conflicts of interest to disclose.
Antibody-Mediated Rejection in Lung Transplant: Pathologist’s Perspective

Prodipto Pal, MD, PhD
Prodipto.Pal@uhn.ca

Rex Michael Santiago, MD
University Health Network
University of Toronto
Toronto, ON, Canada

Antibody-mediated rejection (AMR) is a complex process, well-recognized in kidney and cardiac allografts, but remains ill-defined in lung transplantation [1]. There are no agreed-upon histopathologic diagnostic criteria in pulmonary allografts. AMR as a cause of chronic lung allograft dysfunction (CLAD) is well-established in the literature; yet, the true incidence of pulmonary AMR remains unknown due to lack of comprehensive diagnostic criteria. The consequences of AMR mediated by donor HLA-specific antibodies (donor specific antibodies – DSA) range from persistent/recurrent acute cellular rejection (ACR) to lymphocytic bronchiolitis, and chronic rejection manifesting as bronchiolitis obliterans syndrome (BOS) to the irreversible changes of chronic rejection and CLAD [2, 3].

The pathologic features of AMR are non-specific. The key concept of AMR stems from immune activation and antibody production directed against donor lung antigens by allospecific B-cells and plasma cells, whereby antigen-antibody complexes result in an amplified immune response, mediated by both complement dependent and independent pathways and manifests as transplant associated changes – the pathologic morphological features are reviewed in detail by Berry et al in an International Society for Heart and Lung Transplant (ISHLT) publication [4]. C4d plays a central role in the classification scheme of AMR, which can be detected by immunohistochemistry (IHC) or by immunofluorescence techniques. The spectrum of histologic findings in biopsies, when present, is an indication for further work up for C4d status. The AMR histologic patterns, as mentioned earlier, can be quite diverse. Historically, AMR had been associated with the so-called “hyperacute rejection” where primary graft failure occurred very early post-transplant; morphologically, the findings included fibrin thrombi, fibrinoid necrosis of alveolar septal wall and hemorrhage [5]. Pulmonary capillaritis was the histological mainstay of AMR, although with poor reproducibility [5]. The possible/probable histological findings were later expanded and range from neutrophilic capillaritis to neutrophilic septal margination, high grade ACR or persistent/recurrent ACR, diffuse alveolar damage, high grade lymphocytic bronchiolitis or persistent low grade lymphocytic bronchiolitis (ISHLT grade B2R or persistent B1R), obliterative bronchiolitis and arteritis in the absence of infection or cellular rejection [4]. Interestingly, two additional indications for C4d status included graft dysfunction without morphologic explanation and any histologic finding in a setting of de novo DSA positivity. It should be noted that the aforementioned histologic patterns can be seen in a variety of clinical settings including infection (bacterial and viral), spectrum of ACR, graft preservation injury or reperfusion injuries and secondary to drug reactions.
C4d status determination deserves special mention, as detection of this marker is central to all the recent AMR classification systems. IHC for C4d is an excellent marker for AMR in cardiac and renal transplant patients; however, the interpretation of C4d in lung tissue presents a unique challenge. This can be partly explained by the distinctive microanatomy of lung with multitude of small capillaries, an abundance of pulmonary macrophages, which makes the other markers of AMR detection (e.g., kidney and cardiac allografts) such as CD31 (endothelial marker), CD68 (macrophage marker) extremely difficult to often impossible to interpret. Moreover, since the lung is more often exposed to immunologic challenges (air-borne or hematogenous) as well as infectious or injurious insults, more so than other solid organ transplants (such as the kidney or the heart) further limits an accurate interpretation of C4d. In fact, this hypothesis is indirectly supported by the observation of conflicting results on C4d IHC in pulmonary allograft biopsies [6]. Briefly, C4d staining is reported in interstitial capillaries, vascular and airway elastic fibers, septal walls, venules/arterioles/muscular arteries, peribronchial capillaries, alveolar lining cells and hyaline membranes [7, 8]. The ISHLT recommendation is that the assessment of C4d expression should be made only within interstitial alveolar capillaries, with an immunoreactivity threshold of &gt; 50% to be considered positive [4]. There is limited data in the literature on C4d detection by immunofluorescence on frozen tissue with no specific ISHLT recommendation. The primary objective is to assign accurate subclassification of AMR, without compromising sensitivity; the current recommendation is a multidisciplinary approach using a combination of findings with regard to clinical allograft dysfunction, serologic evidence of DSA, C4d expression and pathologic biopsy findings, reviewed in detail by Levite et al. in a recent article, wherein clinical/subclinical AMR were diagnostically categorized in three categories, viz., definite, probable and possible, based on aforementioned clinicopathologic parameters [1].

With evolving technologies coupled with considerable clinical interest in defining pulmonary AMR, the research opportunities are immense, specifically in elucidating a more comprehensive assessment of biological pathways and towards facilitating more reproducible diagnosis. Newer approaches include gene expression data in a panel of immune regulatory genes using microarray technologies [9]. DSA-induced immune responses operate by activating complements, recruiting natural killer (NK) cells and monocytes, while, the complement-independent DSA operates predominantly via monocyte recruitment (reference). An approach interrogating the biological pathways, specifically the role of NK cells, typable by CD16 IHC, along with downstream interferon-γ induced increased endothelial expression of major histocompatibility complex (MHC) is appears quite promising. Other studies have employed a combinatorial approach of flow cytometric characterization of peripheral blood mononuclear cells (viz., monocytes) in combination with tissue based morphologic findings [10].

In summary, a practical definition and consensus pathologic criteria towards facilitating reproducible diagnosis is critical to further our understanding of AMR.

Disclosure statement: The authors have no conflicts of interest to disclose.
References:
Tweeting at #ISHLT2017

Want to get even more out of ISHLT 2017? Twitter can help!

Reading on Twitter about what others are learning in sessions is the easiest way to start. If you’re new to Twitter, CLICK HERE for easy to understand information on how to set up a Twitter account, how to read what others are posting, and how to post your own comments.

If you want to really engage, you can share comments about what YOU are learning. Share your conference experience and use #ISHLT2017 to connect with attendees, build professional relationships, uncover ideas, spark inspiration, and help others!

A #ISHLT2017 Twitter feed will be scrolling across the bottom of the mobile meeting app home page all day every day to provide real-time commentary and information.
ISHLT 2017 Grants & Awards Winners Announced

We would like to congratulate the following people on being the recipients of the 2017 ISHLT Grants and Awards:

**ISHLT Annual Scientific Meeting Travel Grant**
- Nader Aboelnazar
- Vanessa Blumer
- Mary Bradbury, PharmD
- Hong Chew, MD
- Timothy Gong, MD
- Samson Hennessy-Strahs
- Lisa Hofste, BSc
- Teruhiko Imamura, MD, PhD
- Amit Iyengar, MS
- Takashi Kanou
- Rebecca Kelly
- Liran Levy, MD
- Hasina Maredia
- Ei Miyamoto
- Daisuke Nakajima, MD
- Annelore Sacreas
- Amrit Singh
- Wiebke Sommer, MD
- Jaimin Trivedi, MD, MPH
- Jennifer Woodburn

**Joel D. Cooper Career Development Award**
- Keki Blasara, MD

**Norman E. Shumway Career Development Award**
- Nicole Valenzuela, PhD, D(ABHI)

**ISHLT/O.H. FRAZIER AWARD IN MCS TRANSLATIONAL RESEARCH Sponsored by HeartWare**
- Yasuhiro Shudo, MD, PhD

**NHSAH Research Grant**
- Samantha Anthony, PhD, MSW

**Research Fellowship Award**
- Ramiro Fernandez, MD

**Transplant Registry Early Career Award**
- Laith Alshawabkeh, MD, MSc
- Yuka Furuya, MD
- Christian Heim, MD
- Monique Robinson, MBBS, MRCP, DPhil
- Lorenzo Zaffiri, MD, PhD
2017 Council Meetings and Networking Receptions

**BASIC SCIENCE & TRANSLATIONAL RESEARCH**

**Council Meeting**
Friday, April 7 from 11:30AM – 1:30 PM
(Seaport F-H)

**Council Networking Reception**
Friday, April 7 from 5:45 - 6:45 PM
(Harbor Terrace)

**CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION**

**Council Meeting**
Wednesday, April 5 from 6:15 – 7:15 PM
(La Jolla AB)

**HEART FAILURE & TRANSPLANTATION**

**Council Meeting**
Friday, April 7 from 11:30 AM - 1:30 PM
(Grand Hall B)

**Council Networking Reception**
Wednesday, April 5 from 6:15 - 7:15 PM
(Seaport Terrace)

**INFECTIOUS DISEASES**

**Council Meeting**
Wednesday, April 5 from 12:30 - 2:30 PM
(Coronado A-C)

**Council Networking Reception**
Wednesday, April 5 from 6:15 - 7:15 PM
(Seaport Terrace)

**JUNIOR FACULTY & TRAINEES**

**Council Meeting**
Thursday, April 6 from 7:00 – 8:00 AM
(Gaslamp A-C)

**Council Networking Reception**
Wednesday, April 5 from 6:15 - 7:15 PM
(Coronado Terrace)

**MECHANICAL CIRCULATORY SUPPORT**

**Council Meeting**
Thursday, April 6 from 12:30 – 2:00 PM
(Grand Hall A)

**Council Networking Reception**
Thursday, April 6 from 6:15 - 7:15 PM
(Seaport Terrace)

**NURSING, HEALTH SCIENCES & ALLIED HEALTH**

**Council Meeting**

**Council Networking Reception**
PATHOLOGY

Council Meeting
Friday, April 7 from 11:30 AM - 1:30 PM
(Coronado A-C)

Council Networking Reception
Friday, April 7 from 5:45 - 6:45 PM
(Harbor Terrace)

PEDIATRIC THORACIC TRANSPLANTATION & HEART FAILURE

Council Meeting
Wednesday, April 5 from 12:30 - 2:30 PM
(Seaport F-H)

Council Networking Reception
Wednesday, April 5 from 6:15 - 7:15 PM
(Harbor Terrace)

PHARMACY & PHARMACOLOGY

Council Meeting
Thursday, April 6 from 12:30 - 2:00 PM
(Seaport F-H)

Council Networking Reception
Thursday, April 6 from 6:15 - 7:15 PM
(Coronado Terrace)

PULMONARY HYPERTENSION

Council Meeting
Wednesday, April 5 from 12:30 - 2:30 PM
(Grand Hall D)

Council Networking Reception
Thursday, April 6 from 6:15 - 7:15 PM
(Harbor Terrace)

PULMONARY TRANSPLANTATION

Council Meeting
Thursday, April 6 from 12:30 - 2:00 PM
(Grand Hall C)

Council Networking Reception
Thursday, April 6 from 6:15 - 7:15 PM
(Harbor Terrace)
Nobel Prizes, Transplantation and the Immune System

Javier Carbone, MD, PhD
Complutense University
Madrid, Spain
javier.carbone@salud.madrid.org

Immune response during transplantation is quite complex. Several components participate in distinct phases before and after transplantation and there’s a huge amount of variability. Here, we briefly review more than a century of accomplishments in studying some of these components by Nobel Prizes in Physiology or Medicine. Each of these discoveries have provided us with a better understanding of how this system works.

Emil von Behring (Nobel Prize in 1901) identified serum specific factors that neutralize the toxic products from tetanus and diphtheria bacteria. Specific hyper immune immunoglobulins can now be used for a better control of severe infectious complications after transplantation.

Ilya Ilyich Mechnikov (1908) identified phagocyte cells and phagocytosis. However, the role of this important, innate immune function in heart and lung transplantation remains poorly explored.

Paul Ehrlich's side-chain theory (1908) proposed how antibodies released in blood can control infection.

Charles Richet (1913) discovered anaphylaxis, a life-threatening allergic reaction, as one of the first evidences that the immune system can damage its host.

Jules Bordet (1919) described serum factors that work with antibodies to destroy bacteria: The complement system. Complement factors are now extensively investigated as biomarkers of rejection and infection risk in heart and lung transplantation. Recent work indicates that complement activation regulates key metabolic pathways, and thus, can impact cellular processes, such as survival, proliferation, and autophagy.

Karl Landsteiner (1930) discovered human blood groups. His system for typing blood allowed blood transfusions to be performed without the risk of adverse reactions.

Sir Frank MacFarlane Burnet and Peter Medawar were awarded the Nobel Prize in 1960 for their contribution to the understanding of the concept of acquired immunological tolerance.

Two scientists independently deciphered the chemical structure of antibodies: Gerald Edelman and Rodney Porter in 1972.

Baruj Benacerraf, Jean Dausset and George Snell were awarded the Nobel Prize in 1980. Investigations from these researchers helped to understand the genetic basis of the immunological
reactions, how a specific set of proteins found on the surface of cells (The MHC complex) can regulate this system.

In 1984, Nils Jerne, Georges Kohler, and César Milstein were awarded the Nobel Prize. Jerne’s theories provided a clearer image of how the immune system engages antibodies to fight microorganisms. Köhler and Milstein's techniques for producing specific antibodies helped to create better diagnostic tests and new treatments (monoclonal antibodies).

Susumu Tonegawa was awarded the Nobel Prize in 1987 for his discoveries of the diversity of antibodies and the genetic mechanism for their construction.

Joseph E Murray and E Donnall Thomas were awarded the Nobel Prize in 1990 for their discoveries concerning organ (kidney) and cell (BMT) transplantation in the treatment of human disease.

Peter Doherty and Rolf Zinkernagel (1996) proposed how the immune system specifically recognizes virus-infected cells: The immune system can distinguish foreign agents from its own cells and tissues.

Bruce A Beutler, Jules A Hoffman, and Ralph M Steinman were awarded the Nobel Prize in 2011 for their discoveries concerning the activation of innate immunity and discovery of the dendritic cells and its role in adaptive immunity.

Last year’s Nobel Prize in medicine (2016) went to Yoshinori Ohsumi for his work in cell recycling and discoveries of mechanisms for autophagy. To date, little is known about the role of autophagy in heart and lung transplantation.

Disclosure statement: The author has no conflicts of interest to disclose.
The Spanish Registry of Pulmonary Arterial Hypertension (REHAP)

Jose Cifrian, MD
Hospital University Marques Valdecilla
Santander, Spain
Jose492@separ.es

Recently, large national observational registries in different countries have provided information on current PAH epidemiology, increasing awareness about the disease. Furthermore, these national registries have made possible the reassessment of patient survival under present conditions, leading to the formulation of new predictive survival equations. Epidemiological data from different countries, sometimes with different healthcare organizations, drug availability and financial outreach, may provide a more comprehensive view of current management of the disease worldwide.

Different efforts have been done in United States (U.S Reveal), Scotland (Scottish-SMR), France (French Registry), China (New Chinese Registry), United Kingdom, but also in Spain to try to analyze prevalence, incidence and survival of pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH), and to assess the applicability of survival prediction equations.

The REHAP registry is a voluntary, nonpaid registry that was launched in January 2007. All patients evaluated in 31 hospitals in Spain since January 1, 1998 were included in the registry. Centers reporting patients to the registry covered 15 of the 17 administrative regions of Spain. Patients diagnosed in the period 1998–2006 were entered retrospectively and prospectively thereafter. Data was collected by means of electronic data capture, starting at the initial baseline assessment reported in the medical records. Patients with newly or previously diagnosed PH were eligible for enrolment if they met the definition of PAH and CTEPH and pre-specified hemodynamic criteria by right heart catheterization.

3072 patients have been included in the Spanish registry until February 2017. The REHAP registry is collaborating with important studies in genetic aspects of PAH and phenotypic expression in Spanish population.

The registry is working now in the impact of age on survival of patients with idiopathic and connective tissue disease, pulmonary arterial hypertension, and also in the probable underuse of lung transplantation in severe pulmonary hypertension.

Results of the REHAP registry support the validity of multicenter, international clinical trials and indicate that despite differences in health systems and populations, the evolution of the disease is quite homogeneous when access to advanced specific therapies is guaranteed.
Registries have been extremely helpful in improving our understanding of PAH. It is clear that more registry data will be needed to answer emerging questions.

Since the pioneer NIH Registry of PAH, recent information gathered from national (REHAP) and international registries have shown changes in PAH phenotypes and outcomes in the management of these patients.

Disclosure statement: The author has no conflicts of interest to disclose.
Organ Procurement Surgeons: A Viable Surgical Specialty?

Roger Evans, PhD  
President/CEO  
The United Network for the Recruitment of Transplantation Professionals  
Rochester, MN, USA  
Evans.Roger@Charter.net

Over the past year, I have received numerous inquiries related to the recruitment of what are being called “organ procurement surgeons.” I have come across 10 to 12 position postings on various electronic job boards. With one exception, the postings have only referred to cardiothoracic organs.

Employer of Record: For the most part, the positions have been posted by hospitals and medical centers offering transplant services. In one instance, the position was posted by an organ procurement organization (OPO), in cooperation with a university medical center. Some of the other postings mention the local OPO, without elaboration.

Responsibilities and Duties: The responsibilities of the organ procurement surgeon are variable. Some positions are clearly organ procurement only. In other words, there are no patient care/transplant responsibilities. Thus, the procurement surgeon only has a relationship with deceased organ donors. However, there are variations. Some organ procurement surgeons may also function as a first surgical assistant, and might be expected to provide extracorporeal oxygen membrane oxygenation (ECMO). This, in turn, means the organ procurement surgeon has a relationship with deceased organ donors, as well as patients requiring clinical care.

Qualifications: It goes without saying, organ procurement surgeons must be medical doctors. However, it’s noteworthy that some transplant centers and OPOs use physician assistants (PAs) for purposes of deceased donor organ procurement. Some PAs function independently of physicians and surgeons. Others assist physicians and surgeons in the procurement of deceased donor organs. This clearly raises several questions regarding the credentials of advanced practice providers. I will not address them here.

Licensure and Board Certification: Licensure and board certification are critical considerations for organ procurement surgeons. Requirements potentially differ by state, but certainly by scope of clinical practice. In this regard, I have created a simple table to emphasize what may be necessary.

<table>
<thead>
<tr>
<th>Scope of Clinical Practice</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased organ donors only</td>
<td>Yes</td>
</tr>
</tbody>
</table>
As shown in the table, if a surgeon solely procures deceased donor organs, and has no patient care responsibilities, only a medical license may be required. Alternatively, if the organ procurement surgeon also has patient care responsibilities, board certification will most likely be required.

**Appointment Type:** Based on the position descriptions, most organ procurement surgeon positions are temporary or intermittent, sometimes part-time, and relatively insecure. Surgeons may simply be called upon as needed. In other words, they’re on-call without a schedule.

Appointments at academic health centers are usually at the “instructor” level, without tenure and faculty privileges. Group practice appointments are typically at the “associate” level, not the permanent staff level (sometimes referred to as the “consultant,” or “voting staff” level). Consequently, organ procurement surgeons are expendable, and can be readily relieved of their duties. In many cases, organ procurement surgeons are appropriately described as, and essentially function as, “independent contractors.” In fact, there are a few examples of organ procurement surgeons who are independent contractors, and are paid accordingly.

**Compensation:** As expected, compensation is on the low end. I have seen organ procurement surgeon positions posted with a salary figure of $150,000 annually. This is unrealistic. There are transplant professionals without medical degrees who are paid a much higher salary with generous benefits, and enviable job security. Meanwhile, junior cardiothoracic transplant/MCS surgeons typically make $500,000 or more annually.

**Future of the Position:** Based on the foregoing, the typical organ procurement surgeon position is unattractive for most individuals. Consequently, individuals who may be interested most likely fall into one of several categories, including the following: (1) They could be junior people who have not been offered a suitable permanent position. They, in turn, see organ procurement as a temporary employment opportunity until they can get a “real job.” (2) They might be individuals who have international credentials and, thus, have been denied positions requiring board certification. However, despite this, they may be able to obtain a restricted or specialty medical license allowing them to procure deceased donor organs. (3) They may be surgeons with organ procurement-related research interests who see the procurement of deceased donor organs as a means to further their research.

Based on the foregoing, I’m skeptical of the long-term viability of surgeons whose sole responsibility is procurement. Alternatively, I think cardiothoracic surgeons should be recruited with the understanding that a disproportionate share of their clinical practice will be dedicated to organ procurement. In addition, depending on their skill set, they will be routinely involved in the care of patients with advanced cardiovascular and pulmonary disease. Furthermore, based on their skills, they will have an opportunity to perform general cardiothoracic surgery, transplant
procedures, implant mechanical circulatory support systems, and participate in the initiation, maintenance, and discontinuation of ECMO/ECLS.

Disclosure statement: The author has no conflicts of interest to disclose.
Cardiac Surgeon, Generic University Medical Center, Division of Cardiac Surgery, Any City, Any State, USA

Description:

Generic University Medical Center, Division of Cardiac Surgery, is actively recruiting a cardiac surgeon with an academic appointment commensurate with experience.

As everyone knows, we’ve been recruiting forever. Our position is moribund, and we’ve recently decided it’s pretty much dead. Nonetheless, we’re giving it the old college try. We know football fans will appreciate our commitment, although we’re obviously losers. Without explanation, people have simply quit our A-team, as well as our practice squad. Thus, we now ask that you forgive us for past transgressions. We’re on a bumpy road to recovery. With each additional setback, we’re committed to digging a little deeper, until we reach six feet.

The ideal candidate will have experience in minimally invasive cardiac surgery, including robotics, valve and coronary surgery, as well as TAVR. LVAD/MCS and transplant experience is preferred.

A robust academic environment within a unique Heart and Vascular Center exists for the qualified candidate with a desire to participate in collaborative clinical, educational, and research activities. Conflict instigation will not be tolerated. It undermines productivity, yielding negative RVUs. In this regard, slackers are unwelcome.

Successful candidates will be ABTS board-certified/board-eligible, and will have successfully completed an ACGME-approved surgery residency with three to five years post-training experience. A medical license is required, but will not be verified.

This is a last gasp effort to attract a qualified candidate. Consequently, the Division of Pulmonary, Allergy, and Critical Care Medicine is playing a major role in this recruitment effort. We concede ECMO may be required, although reimbursement could be an issue. Obamacare is no longer a refuge for extreme measures. However, by the same token, with Republicans rejecting the so-called Obamacare “death panels,” we may have a future after all. Unfortunately, it’s clear things could get trumped-up along the way.

With one exception, Generic University Medical Center is committed to affirmative action, equal opportunity, and the diversity of its workforce. The exception is as follows: dead-on-arrival (DOA) candidates are considered unacceptable, and will be rejected. However, as a show of good faith in our recruitment efforts, we will provide caskets for the deceased. Unfortunately, we are unable to offer a proper burial/funeral service, but all other benefits will accrue, including pallbearers upon request. In this regard, for a small fee, the Medical Center CEO, CFO, CMO, Director of Patient Experience, the University President, the Dean, the Division Chief, and assorted incompetent
administrators and human resources representatives are available to provide a little heft to the lift off. Since you can’t get us to where we want to be, we’ll get you to where you’re going.

Disclosure statement: The author has no conflicts of interest to disclose.
EDITOR’S CORNER: Dealing with Death as Witnesses

Vincent Valentine, MD
University of Alabama Birmingham
Birmingham, AL, USA
Vvalentine@uabmc.edu

Out of referrals, evaluations, listings and replacement procedures including transplantation and deploying mechanical devices, along with ongoing care and dutiful management comes experience with recovery and death. The thousands of lives we touch regardless will still result in the unavoidable topic of death. It is the pillar that underlies medicine, life, and art. We must turn to the literary arts to add a human dimension of our endeavors in medicine and life. If there is one book that will guide us among many others, it is *Intoxicated by My Illness and Other Writings on Life and Death* by Anatole Broyard. I believe it is the ultimate must read for all health care providers, especially for the ISHLT. We will benefit from the enlightenment that art can offer. Witnessing death has and will continue to occur, yet do we know what it means to witness death? To what extent is death a reality more for witnesses than it is for the dier?

Faulkner’s book *As I Lay Dying* sets the stage of death. In it, Dr. Peabody says “I can remember how when I was young I believed death to be a phenomenon of the body; now I know it to be merely a function of the mind—and that of the minds of the ones who suffer the bereavement. The nihilists say it is the end; the fundamentalists, the beginning; when in reality it is no more than a single tenant or family moving out of a tenement or a town.” Faulkner illustrates this dynamic picture of death as a form of mobility. In conjunction with these mind and body components, great literary works offer various dimensions that allow us to examine death from different perspectives. While an individual cannot suffer death and then be expected to describe it, art is capable of exploring and addressing all viewpoints of the deceased. We might ask: Who are we in nature’s vineyard? How do we experience death, in what ways, and at what distance? Are we the one who dies? Are we the loved one who tends the death of someone? Are we the physician who manages someone’s terminal illness? The bystander or the taxpayer, who will pick up the bill? Dying is expensive. In our efforts to resuscitate and support patients through recovery and rebirth, we must bear in mind that our other duty is to recreate or tell the story of a dying patient in effort to maintain their dignity. Also, bear in mind reconstructing the meaning of a person’s life as a measure of their death, or the meaning of a person’s death as a measure of their life will secure dignity, grace and humanity.

The death story of someone we know is vastly different from that of someone we don’t know. Moreover, the death story of someone we know is actually our story. Anatole Broyard’s *What the Cystoscope Said* is a trying, demanding, emotional and brutal story of the death of a son’s father. Told from the son’s point of view, Broyard prompts readers to question: how do we let go of someone we know?

We all yearn to age gracefully and die with dignity. Further, we are stripped of our entitlements in death or during the act of dying. The son tries to share the workload in hopes to become a man
and measure up to his father; a foreman and carpenter. The father’s entitlements were his physical strength, pride, and virility; however, Broyard reminds us that patients are yoked by disease as he sets the tone in the opening lines. He opens, “When I saw my father with the horse collar around his neck, I knew immediately.” Being yoked, the father experiences a servitude he has never known before (A neck collar prescribed for neck pain from metastatic disease, also note hidden racial overtones). Along with his integrity and authority, his physical strength is now inadequate. While the father is accompanied by his dutiful son, the doctor uncaringly talks with him to get the inside story. “We have a little surprise... We want to get the inside story on you, so we’re going to give you a cystoscopy. They can be sometimes be unpleasant, but I don’t think that will bother an old soldier like you.” This is the inside story of dying, or of a son witnessing his father’s death. The test is performed and completed, and Broyard offers brilliant metaphoric language, a manifesto of the experience of having undergone cystoscopy.

The son arrives in his dying father’s hospital room and registers his own disbelief. The nurse says, “Your father is in there.” His quick response, “But my father wasn’t in there.” The son describes his father “Sprawled on a table, incredibly out of place, lay a plaster Prometheus, middle-aged and decrepit, recently emptied by an eagle, varnished and highly glazed as though still wet... Or perhaps... an eviscerated old rooster, plucked white, his skin shiny with a sweat more painful than blood.” Broyard uses sexual and racial overtones to illustrate an impotent cock being plucked white. The son reflects saying, “Whatever it was, it wasn’t my father. It might have been an old man, trembling and staring into eternity, whom I helped, avoiding the puddles of his exploded bladder, to dress and who staggered out on my arm, but he was not in the least like, bore no resemblance whatsoever to, my father.” Here, Broyard utilizes metaphor as a powerful tool to represent suffering of the physical body.

Many writers try to find a language representing the felt experience of those aspects of illness underrepresented by such narratives. The description of physical pain, emotional suffering, and the way bodily damage affects the self and other aspects of illness are indescribable including grief, despair, terror, and especially death.

When the attending physician tells the son “The cancer has reached his bones, I’ll give him six months.” The son wanted to say, “Why will you only give him six months?” But all he could ask is “Are you going to take him in as a patient?” The doctor removed his pince-nez and responded, “We don’t keep incurable cases.” The son with Broyard’s classic humor quipped – “No, you send them packing.” Then he bit his lips to stop hysterical laughter. The art of creating such vocabulary to describe pain, suffering, and death is difficult. Pain is the key secret on how to find the words to tell the story. How to understand that someone’s death is not just the utterances from the sufferer entering death, but rather a story that has a shape. Death is the relationship of the living and the dying, those who are left with those who leave- and by its own authority, we know very little about it. The inside story is not limited to those who have died, it will happen to every person who lives and we are uniquely positioned as members of the ISHLT to tell these stories.

The loss of the father’s stature prepares the son to take his place. Like most death stories, this is one about the coming of age for sons and daughters. Diving deeper, Broyard’s What the
Cystoscope Said demonstrates yet another obvious story, involving nurse and patient/family relationships. With the nurse’s help, the son is able to deal with the internal suffering caused by the death of his father. The nurse is described as an “advertisement of life in this gray ward of old men with erectile dysfunction.” Broyard explains that “...by sympathetic magic he resuscitates...” his father and the other failing men who view the nurse tending them in their hospital ward “...more mirage than oasis.” The son asserts his virility in a dominating way as he performs a service for his father and these other impotent men who are deprived of their dignity, strength and power. In this hospital or any hospital today, we are reminded how decimating growing old, weak, and dying is, in terms of strength and virility. In terms of transplantation, our patients are rejuvenated; they have a new life or a new lease on life, a rebirth.

With death or the dying self, writers frequently refer to darkness, another location, tenement or country as unfamiliar grounds. Thomas Wolfe wrote: “I’ve made a long journey and been to a strange country, and I’ve seen the dark man very close.” In Robert Frost’s poetry we have, “I have been acquainted with the night” while F Scott Fitzgerald writes, “in the dark night of the soul it is always three o’clock in the morning.” Night is the time when fear of death takes over and metaphorically, it is the time when a person encounters his or her darker feelings. Some are afraid of the dark and some are afraid to die. When death is expected with relatively little pain, people think and describe their feeling about dying in language. However, when someone is wracked in pain in the throes of death, language ceases to be a possibility. Uttered random words or sounds devoid of meaning such as a cry moan, or shriek may come out. This is probably why we have no description from a person who is dying of what this experience is really like. All we can do is witness the dying person or dying body.

How do we let go? Do we remain "Frozen.” This process is described as mourning. Freud writes “when someone that we love dies, we learn not by volition, but by reality. We learn to sever the connections and remove the ego’s attachment from the person who is no longer alive. This is a difficult procedure that takes a long time. All bonds uniting us to our loved ones must be brought up and cut one by one - mourning. Once severed, the ego becomes free and uninhibited then by nature and not by morality. Then, the ego attaches itself to something else. Living organisms maintaining connections with something no longer real learn to cut their losses.” Freud’s definition of mourning promotes the modern self to simply sing “Let It Go” like Elsa from the Disney Pixar Movie.

In stark contrast, Linda Pastan’s moving poem “The Five Stages of Grief” focuses on the reality principle challenging Freud’s theory. She suggests that the memory of loss is a reversal to cutting bonds or letting go. A memory is a way of making sacred the emotions retained from a lost love. When those we know and love die, they never die in us. Told from the perspective of husband and wife, readers witness death and its altering affect. In oneself, after the death of a significant other, one is changed through mourning. I have lost you.

Moving from a child or spouse witnessing death to the actual dier, we turn to Tolstoy’s The Death of Ivan Ilyich. Ilyich’s death begins like most deaths, as a newspaper event. We learn about the deaths of most people we know in the obituary column.
Like a son who takes the place of a father after death, someone else can take their place within the bureaucracy of the workplace or society. Upward mobility depends on death; therefore, death is not just a moral issue, it is Faulkner’s mobility. There are also economic issues and pragmatic moves that occur.

Moreover, death is embarrassing. How do others, friends, and love ones behave during death? How do you conduct yourself?

Ilyich’s lives a bland and secular life. He follows the rules. He does the right thing and goes through life in a perfunctory fashion. Like most people today, he is incapable of separating his job duties from his private life. Then Ilyich sees a new rival order in life with his wife’s pregnancy. This disturbs him. There are childhood illnesses, life becomes messy and some of his children die. To cope with these changes, he shifts his focus further away from his family and towards his work as an escape. While moving into a new house and decorating he climbs a ladder and falls...“the biblical fall,” then the pains begin and never go away. The physicians he turns to were not helpful. Not one of them addressed how serious his condition was and if he was going to die. The doctors’ professionalism and conventions of their own field and mundane routine were no different than his. They ignored his dilemma. Towards the end, he realized he did not actually live. In the end, he suffers through three days of screaming then “he sees the light.” He has acquired humility and generosity then enters a peaceful acknowledgement of death. In this story of dying is a story of living and a man’s discovery that he has not live at all.

Disclosure statement: The author has no conflicts of interest to disclose.