

VINCENT'S TWO SENSE

The ISHLT exceeds disciplinary borders with involvement from more than one specialty including cardiothoracic surgery, cardiology, pulmonary, pediatrics, pathology, immunology, basic science, basic science, infectious diseases, nursing, social work, psychology, other allied health areas, pharmacy, and the many personnel maintaining the ISHLT. The extended borders are across space, countries, regions, cultures and time. With such immense diversity, the Society has exposed and educated its members on vast skills and new patient technology such as heart transplantation, lung transplantation, ventricular-assist devices, extracorporeal membrane oxygenation, other forms of mechanical circulatory and respiratory support including advances in donor management. It is important to celebrate the success caused from new research, as it is communicable to the curiosities of other's. Keeping mindful of accomplishments of the past continues to remind us that it is not history that repeats itself but the behaviors of men and women who repeat history so we dare not make the same mistakes. The new mistakes are enough.

In this issue, we have congealed as a society and continue to take the impact factor of the Journal of Heart and Lung Transplantation to new heights. David Baran of Sentara Hospital in Norfolk, VA extols are impact factor of 7.11. We have lost a great pioneer of heart and lung transplantation from France, Christian Cabrol. This issue pays homage to him as one of our giants and his illustrative career. Dr Brandon Larsen from the Mayo Clinic in Scottsdale, AZ and Dr Diyar Saeed of Hinrich-Heine University in Dusseldorf, Germany, Dr Palak Shah of Inova Fairfax Hospital in Virginia and Dr Jennifer Cook of University of Arizona in Tucson, Arizona provide updates from the Pathology Council and MCS Academy 2018, respectively. Dr Jorge Silva Enciso of UCSD in San Diego representing the Junior Faculty Council delivers an insightful update on heart-lung transplantation for congenital heart disease and challenges our math with the sum of one and one. Javier Carbone, our Ambassador of the International Correspondents Board from Complutense University in Madrid reminds us of the growing problem of secondary immunodeficiencies of our patients we manage. It is Sara Schlette, MCSD Coordinator from the Mayo Clinic in Rochester, MN, who links us with Words, Books and Patients to help us manage complex and challenging problems in our patients as we balance to do the right thing and maintain their trust and confidence. Finally, yours truly from the Editor's Corner evokes the ancients to start a wisp of a journey through the evolution of natural philosophy to science over hundreds of years and what it means to us today as we look ahead to the 38th Annual Meeting in Nice, France.

IN THE SPOTLIGHT: JHLT Impact Factor: Take it to the Top

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Discoveries and advances in medicine occur with increasing speed; therefore, textbooks serve to provide a foundation for knowledge. We rely on journals to inform on the latest and greatest developments, many of which are able to be translated into clinical practice. Health care providers must read journals to adhere to the rapidly evolving fields of medicine including Heart failure, thoracic transplantation and mechanical circulatory support. There are numerous competing journals all vying for the reader's eye.

A logical place to acquire the latest information in these areas is the Journal of Heart and Lung Transplantation, which is the official Journal of the ISHLT. This has always been a key journal to read about the annual ISHLT Registry Report as well as immunosuppression for both heart and lung transplantation. However, under the leadership of Dr. Mandeep Mehra in recent years and Dr. James Kirklin prior, the JHLT has grown substantially housing influential papers on mechanical circulatory support and increasingly for matters of pulmonary hypertension and advanced lung disease.

The key way journals are ranked is by impact factor, which is derived from the quantitation of how many articles reference publications in the journal. Like re-tweets, shares on Facebook, or views on YouTube, this is the professional index of relevance and impact on the field. The impact factor of the JHLT has had a meteoric rise of late, and now our journal is the number one transplant journal in terms of impact, with a score of 7.11 out of a field of 56 other journals. In 2016 alone, JHLT articles were cited more than 3200 times by other articles! In a field of 372 journals of surgery, the JHLT is the 3rd highest impact surgical journal alongside the Annals of Surgery and American Journal of Surgical Pathology.

This is a stunning accomplishment which drives further success. After all, as authors we all want to send our original research to the "best" journal, and it is so exciting that our Society's journal is indeed confirmed to be the highest impact.

It is a great time to be involved in ISHLT, and to send the best work in abstract form for consideration at the Annual Meeting. Accepted abstracts may be submitted as full length manuscripts, or research correspondence to the JHLT and potentially have access to the broad audience of the journal. With such high impact science being published monthly, acceptance in the Journal is tough to achieve, but nothing worthwhile is ever easy. We owe it to our patients and our field to be certain the latest and best work appears in our Journal!

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Update from the Pathology Council – Recap of 2017 Annual Meeting

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Although we are only a small subset of the broader ISHLT membership, 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 to help the patients we serve! This past April, we enjoyed a highly productive Annual Meeting, where we were enriched not only by great scientific content, but also by the close comradery of our excellent colleagues. At this meeting, we saw a renewed emphasis on several Council initiatives and heard several new proposals aiming to expand our research and educational efforts as we seek to improve the care of our patients and enhance the skills of our pathology colleagues who are not (yet) members of the Society. We also witnessed a change in leadership in our Council, with Dr. Robert F. Padera assuming the role of Council Chair for the next two years, and Dr. Martin J. Goddard stepping down and assuming the role of Council Past Chair. We are grateful to Dr. Goddard for his leadership and service, and look forward to having Dr. Padera at the helm!

Pathology Council Initiatives

The Pathology Council remains committed to educational initiatives, and several were discussed at the Annual Meeting. In particular, members of the Council 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 on cardiac ACR and AMR for pathologists, including online quiz components, in partnership with the Society for Cardiovascular Pathology and Association for European Cardiovascular Pathology (<http://scvp.net/acr/index.html>). Members of our Council are also developing online tools to aid pathologists in interpretation of lung transplant biopsies. Our European colleagues led by Dr. 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, but is coming together nicely. If you encounter good examples of diagnostic grades of rejection or other entities that could be included in this online resource, please contact Dr. Calabrese at fiorella.calabrese@unipd.it. Both of these online resources continue to be well received, but suggestions for improvement are welcome. Not to be outdone, Dr. Dylan Miller is continuing his legacy as a computer guru and developer of fine online tutorial products, and reported his progress on a new online "eQA" resource and aid for heart transplant biopsy interpretation. Although still under development, this promises to be a highly useful and practical resource where scanned slides can be reviewed for educational purposes and compared with interpretations of other users, perhaps also including a quiz component. Stay tuned...

A number of research initiatives were also discussed at the Annual Meeting. Dr. Gerry Berry, Dr. Jean Paul Duong Van Huyen, and colleagues are forging ahead with a project investigating inflammatory burden in cardiac AMR in collaboration with other institutions, and this project is ongoing. Hopefully, this project will shed some light on the significance of different inflammatory components in heart transplant biopsies. This group met earlier in Washington, D.C. and subsequently in San Diego, and the project is moving forward as they accrue patients with rich clinical information and DSA data. There is also interest in developing research projects investigating the significance of intravascular versus extravascular inflammatory cells in this context, as well as studies evaluating reproducibility in interpretation of heart transplant biopsies. Perhaps Dr. Miller's "eQA" platform will also aid in these efforts, and we hope to see many of you participating in these efforts.

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. With this in mind, the Council discussed ways to increase our membership and to better understand the barriers preventing others from joining our group. Ideas included a suggestion to establish a best poster award, to be given as part of our Annual Meeting to a trainee or junior member, as an incentive to increase participation in the Council. It was also suggested that we re-attempt to reach transplant programs that lack an ISHLT member pathologist, as Dr. Goddard attempted last year, in an effort to hopefully connect with and attract future members. It was also suggested that a survey of transplant pathologists may be useful to illuminate the issues and barriers preventing others from joining. Again, perhaps Dr. Miller's "eQA" platform might provide another solution for some of these challenges, perhaps offering additional incentive or value for prospective members. These issues will undoubtedly remain topics of discussion over the coming year. However, we also 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.

Recap of 2017 Annual Meeting and Scientific Sessions in San Diego, CA

It was great to see many of you at the Annual Meeting in April, and those who were there enjoyed a rich and dynamic agenda, including several excellent pathology-oriented sessions. Although there were many great sessions throughout the week, this year saw an important change in the format of the meeting, whereby program content relevant to the Pathology Council was clustered into a single day (Friday), instead of being distributed throughout the entire meeting over several days. This concentration of program content shortened the time required to attend the meeting for many of us, and was generally well received. Hopefully, this concentration of content into a shorter time period will provide additional incentive for those who wanted to attend in the past, but could not due to time constraints. Please spread the word to your non-member colleagues about this change, so we can hopefully see more pathologists in attendance next year.

For those of you who were not able to attend, this year's meeting included an excellent Sunrise Symposium on mixed rejection in the cardiac allograft, which remains a challenging and somewhat controversial topic and is certainly deserving of more attention and research. Although this was early in the morning, it packed several highly informative talks into a single hour and was well attended. Our Council also hosted an Oral Session the same day, discussing various diagnostics in heart and lung transplantation. Lastly, there was an excellent moderated Poster Session in the evening that highlighted a number of important ongoing studies from many of our Council members... and most importantly, included a wine and cheese reception! These sessions were energizing and we look forward to seeing many of you at the next annual meeting, April 11-14, 2018 in Nice, France. Mark your calendars.

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When One Plus One Does Not Equal Two

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Combined heart and lung transplantation has been sought as the therapeutic option for patients with advanced pulmonary vascular disease including congenital heart disease, fixed pulmonary hypertension with elevated pulmonary vascular resistance (PVR) or idiopathic pulmonary arterial hypertension. The recent ISHTL registry data contains more than 3800 combined heart-lung transplants (HLT) worldwide but the number of HLT performed has decreased in recent years probably due to advances in technology and pharmacological treatments for such patients. Many patients with fixed or irreversible pulmonary hypertension from left heart disease for example are candidates to receive a ventricular assist device as a bridge to transplant with the goal of reducing PVR. Patients with IPAH are improving quality of life, functional class and survival with targeted medical therapy. For CHD patients, however therapeutic options are limited once advanced heart failure occurs. The ISHLT registry notes that CHD is increasingly one of the most common reasons for HLT (35% for CHD, 27% for IPAH and 11% for cardiomyopathy) although survival for HLT has been lower compared to heart or lung transplant alone (HLT survival: 71% at 3 months and 63% at 1 year; lung transplant: 89% at 3 months and 80% at 1 year; heart transplant: 89% at 3 months and 85% at 1 year based on registry 2009-2014 data) [1]. Why is it then that despite adding 2 organs survival is still poor? To date there is paucity of data related to the risk factors associated with mortality in HLT. Some registry studies have found preoperative factors that may impact postoperative outcomes. Kadakia et al. analyzed the long and short term survival of 571 HLT recipients from the United Network for Organ Sharing database over the 1993-2009 era. Forty-six percent survived more than 5 years while 54% survive less than 5 years. The results of the analysis showed that male recipient increase the 1 year mortality risk by almost 2-fold. However, the more significant factors associated with 1 year mortality were those patients that underwent preoperative extracorporeal membrane oxygenation (ECMO) with a 7.55 hazard ratio and mechanical ventilation with 3.5 hazard ratio [2]. These findings are not surprising as patients awaiting HLT are a severely complex and sick population that need additional support—mechanical, ventilator, dialysis prior to transplant compared to heart transplant or lung transplant alone recipients. Unfortunately, these measures can increase risk for adverse postoperative outcomes including death. Several causes of death in the early post-transplant period have been found in HLT recipients. Among them, primary graft failure (PGF) is one of the most common ones with 29% of all HLT recipients developing PGF. Other significant causes include technical complications, cardiovascular and multi-organ failure. Related to graft failure possible causes may be due to acute rejection, primary graft dysfunction or other factors early post-transplant. Among factors linked to acute rejection, male gender, CMV positivity, donor infection and class I PRA greater than 10% have been found to be prognostic [2]. In CHD patients undergoing heart transplant, comparable risk factors have been found associated with early post-transplant mortality including donor-recipient CMV mismatch and elevated PRA. The latter is a common finding in CHD patients as many of them have pre-formed HLA antibodies likely from prior corrective or palliative cardiac surgeries which in turn lengthens operative and allograft

ischemic time during transplant surgery. Moreover, the perioperative use of ECMO in this high-risk group is not an uncommon practice that increases overall operative time [3]. Perhaps then, the elevated rate of PGF in the HLT cohort could be related to the elevated number of post-op complications seen early after transplant. The rates of reoperation, need for blood products and dialysis are higher in CHD patients than non-CHD adding further to the risk of future antibody formation in this group [4, 5]. Moreover, ISHLT registry data denote PGF, technical complications and multi-organ failure as the highest causes of death for CHD patients undergoing HLT. Such worrisome outcomes are of concern for future organ allocation of this high-risk population. As the adult CHD population continues to increase and becomes the predominant reason for HLT, we need to be attentive to when appropriately or timely refer patients for HLT and identify the risk factors that increase morbidity and mortality post-HLT. More studies are needed to identify and develop risk stratifying tools based not only on donor or recipient characteristics but also on type of CHD anatomy. Once we recognize the prognostic factors, we will be able to adequately select patients, plan operative needs to reduce postop complications, reduce prolonged ischemic times and tailor immunosuppression for both organs whilst improving survival.

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Christian Cabrol 1925-2017

Christian Cabrol, renowned pioneer of cardiac and pulmonary transplantation, and ISHLT President 1991-92, died on June 16th 2017. He had been ill for a number of months and spent his last days in his own hospital, Pitié-Salpêtrière.

Cabrol was born in 1925, and educated in Paris. He trained in thoracic and then cardiac surgery, spending a year with Lillehei in the USA. He came to prominence when, in 1968, he performed the first cardiac transplant in Europe. His patient lived only 53 hours, but he persisted when others hesitated, seeing clearly the potential for great impact. In the late 1960's and early 1970's, Shumway's team at Stanford and Cabrol's group in Paris were almost alone in keeping heart transplantation alive.

Always in the vanguard, Cabrol went on to perform the first heart and lung transplant in Europe in 1982, and then in 1986 the first implant of the Jarvik 7 total artificial heart.

Cabrol was always welcoming, a great friend to many, supporter of colleagues around the world and influential teacher to many young surgeons. President of our Society in 1991-92, he was still active when ISHLT met in Paris in 2009. A video interview with him at that time can be seen in the ISHLT Archives (<http://www.isHLT.org/historyandArchives/videoInterviews.asp>).

He spent much of his later life active in politics, as a councilor in Paris, member of the European Parliament and finally deputy Mayor of Paris, 1995-2001. Christian Cabrol was a charming Frenchman, a pioneer surgeon and a friend to many who will be remembered with tremendous fondness.

On behalf of the entire ISHLT membership, we send our condolences to his family whilst also celebrating his enormous contribution to our global thoracic transplant community.

Secondary Immunodeficiencies: A Growing Problem?

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Widespread use of biologic therapies and procedures such as ventricular assist devices and ECMO is associated with an increase in the number of patients who can develop secondary immunodeficiency. Indeed, severe and recurrent infections are a common adverse effect of these interventions.

Biologic therapies do not cause the same degree of immunosuppression as that observed with more conventional immunosuppressive drugs, such as corticosteroids, cyclosporine, tacrolimus, mycophenolate, methotrexate, cyclophosphamide, and azathioprine. However, they may have unintended effects on immune function that can compromise innate and acquired immunocompetence and lead to severe infections. Some biologics can also induce other adverse effects of immunosuppression, such as autoimmune diseases and malignancy. The many new biologics targeting the immune system are subject to various infectious complications.

Examples of clinical settings in which biologics are increasingly used include cancer, lymphoproliferative syndromes, autoimmune and inflammatory diseases, and transplantation.

The biologic therapies that increase the risk of infection include antithymocyte globulin, monoclonal antibodies to T and B cells, anti-cytokine therapy, anti-cytokine receptor therapy, and therapies that modulate T-cell costimulation signals. Anti-checkpoint monoclonal antibodies have recently been introduced for the treatment of cancer. In order to achieve their specific effects, these therapies selectively target receptors, cells, proteins, and specific pathways of the immune response.

Factors that increase the risk of infectious complications depend on the mechanisms of action of the biologic, dose, dosing interval, and duration of treatment. The risk of infection also depends on concomitant therapies and surgical interventions and patient-specific factors. For example, heart and lung recipients using ventricular assist devices or ECMO are at an increased risk of infections.

The management of secondary immunodeficiency may include monitoring of the patient's baseline immunocompetence and early detection of secondary immunodeficiency after therapy and the use of prophylactic antimicrobials or immunoglobulin for the treatment of hypogammaglobulinemia.

Intravenous immunoglobulin replacement therapy is approved for severe infections and hypogammaglobulinemia with specific antibody deficiency in patients with multiple myeloma and chronic lymphocytic leukemia. In this regard, a revision of the core summary of product characteristics for intravenous human normal immunoglobulin of the European Medicines Agency is evaluating the current status for their use in other secondary immunodeficiencies including solid organ transplantation.

An update of the management of CMV infection in solid organ transplantation including the potential role of immunological biomarkers for prediction of this complication has been recently performed by an expert group of the Transplantation Society.

Monitoring of the levels of biologics and of the development of antibodies against them is another rapidly evolving area that plays a key role in evaluation of the safety of these drugs.

Patients with ventricular assist devices and ECMO may develop secondary immunodeficiency that places them at higher risk of developing infection. By identifying and controlling risk factors, it is theoretically possible to reduce the occurrence of infections. Management of modifiable risk factors might reduce mortality rates.

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Update from MCS Academy 2018

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The Core Competencies in mechanical Circulatory Support (MCS) began in 2012 under the leadership of David Feldman, Andreas Zuckermann and Jeffrey Teuteberg. Since then and due to continuous positive feedback from conference participants, the academy has been an extraordinary source for education. Traditionally, the academy takes place one day prior to the ISHLT meeting. This course provides a concise review of clinical knowledge and outlines the essential professional skills for candidate assessment and longitudinal support for mechanical circulatory support patients. The course is primarily designed to be of benefit for clinicians and allied professionals who are in the early stages of their careers. The course also provides an update on the current state of the field for more established providers.

Today, the MCS Academy is chaired by Jennifer Cowger, Palak Shah and myself. A tremendous amount of effort was put in to coordinate an excellent program with international leaders. I have really enjoyed working with Jen and Palak, and I have learned substantially under Dr. Cowger's tutelage. Last year, the 234 participants of the MCS Core were surveyed for feedback on the educational experience. In the participants who responded: 9.3% were from Asia, North America 62.5%, Europe 15.6% and 9.4% from South America. Twenty-eight percent were mid-level (5-10 yrs), 28% were recent graduates (1-5 yrs) and 15% were either student / trainees or in post-grad training. Further, 34% from responders were cardiologists, 16% cardiac surgeons, 10% thoracic or vascular surgeon, 9% research fellows, 3% anesthesiologist, 3% nurses and 3% infectious disease staff. Almost every participant gave the course a 4 or 5 on a 5 point scale. Interestingly, the more senior attendees were more satisfied with the case / didactic balance of the course. Based on the feedback we obtained, we can summate that the majority of the participants enjoyed the meeting.

In 2018, I have the privilege of chairing the MCS Core Academy with Palak Shah and Jennifer Cook. The basic program will remain similar; however, we will welcome some new speakers including several international faculties to share the MCS experience from all parts of the world. Just like this year, we are planning to involve world leaders in the field to provide the most up-to-date knowledge on mechanical circulatory support. We promise to maintain the high quality of the Academy and exceed the expectation of academy participants. We are looking forward to seeing you in Nice!

Words, Books and Patients

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A quick shameless Wikipedia search suggests that 45% of English words derive from French origins. French hails primarily from Latin roots, and Latin is the foundation of medical terminology, linking medical providers together in the end with words being our primary sources of communication. When pondering the concept of words, I immediately recalled several interesting concepts I have read in few recent books, one which ironically was bought to tide me over in an airport delay after ISHLT.

Some Links readers may be familiar with “the jam studies,” an interesting assessment of the impact of choices in decision making. Sheena Iyengar in her 2011 book *The Art of Choosing*, describes the study. Large jam assortment stands with 24 flavors and small jam assortments of 6 flavors were set up on different days at the same grocery store. 60% of shoppers were drawn to the large assortment and 40% to the small assortment. Customers could sample as many jams as they wished, and on average 2 jams were sampled regardless of whether the assortment was small or large. Customers were tracked using \$1 discount jam coupons. 30% of those with coupons in the small assortment group bought jams, but only 3% of those with coupons from the large assortment group bought jam. It was concluded that “when people are given a moderate number of options (4-6) versus large number (20-30), they are more likely to make a choice, are more confident in their decisions, and are happier with what they choose.” It may behoove us as clinicians to remember such things when presenting our patients with options as a way to improve their satisfaction in making complex medical decisions.

Amos Tversky and Daniel Kahneman published interesting data regarding framing effect, or reactions based on gains or losses. They reviewed two groups of individuals potentially facing surgery or radiation for whom data was presented in terms of survival (i.e. (A) 90% survive surgery and have a 34% 5 year survival or (B) all survive radiation treatment with a 22% 5 year survival after) or presented in terms of mortality (i.e. (A) 10% die with surgery and 66% have died 5 years after or (B) 0% die with treatment and 78% died 5 years after). Interestingly, and perhaps not surprisingly, in the group for whom data was presented in terms of survival, 25% preferred radiation to surgery, whereas 42% of the group for whom data was presented in terms of mortality preferred radiation to surgery. The authors note, “when the possibility of dying during surgery was highlighted, people were more likely to select radiation therapy, even at the cost of decreased survival.” Criticisms of these findings suggest that implied consequences may unfairly bias participants. Regardless, the concept certainly is thought provoking and may play a role in how we could approach informed consent for medical procedures.

Joseph Hallinan, author of *Why We Make Mistakes: How We Look without Seeing, Forget Things in Seconds and Are All Pretty Sure We Are Way above Average*, describes a study of colostomy patients at MI medical center. Some patients were told there was a possibility of reversal in the future, some

were told they would have a permanent colostomy. Overall life satisfaction over 6 months was tracked. Perhaps surprising at first was the finding that permanent colostomy patients were happier, improved more rapidly and were better adapted than the cohort of colostomy patients with possible reversal who remained relatively unsatisfied. Hallinan notes that, "hope impedes adaptation...if you're stuck with something; you learn to live with it. And the sooner you learn to live with it, the happier you will be." I found this particularly thought provoking in the context of mechanical support device patients and the categorization of patients as bridge or destination therapy and how waiting for a transplant that has not yet been realized compared with permanent therapy may affect overall satisfaction.

Schooler et. al. published an article in Cognitive Psychology in 1990, aptly titled, *Verbal Overshadowing of Visual Memories: Some Things Are Better Left Unsaid*. He categorized individuals into two groups both which were shown paint swatches. The first group was asked to describe the paint color and the second group was asked to merely look at the paint swatch. Afterward, both groups were shown 6 swatches and asked to pick the original paint swatch that they were shown. 73% of non-describers were correct compared with only 33% of describers who were correct. He concluded that "verbal descriptions of experiences can overwrite memories of experiences (thus) remembering not what they had experienced but what they had said about what they experienced...we reduce experiences to words." Verbal descriptions from memory of a past event, treatment or hospitalization are merely recapitulation of what we recall a memory to be. This may be worth noting as we all can recall patients who relive their medical experiences and perhaps in a way, end up with the memory that they want.

These and many other books and articles have caused me to pause and assess how I offer care and treat patients. Overwhelmingly, patients with options may result in dissatisfaction. Rather than clearly offering fewer options, phrasing surgery in terms of survival versus mortality may impact what my patient may choose, and hope may be a double edged sword in some situations. How fortunate we all are to have patients place their life and care to us as providers, and it is my hope that we all consider the responsibility that this entails and remain good stewards of our patients trust and confidence.

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EDITOR'S CORNER: Geocentric, Heliocentric, Eccentric and Egocentric Revolution of Science

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Science is a systematized knowledge that has been accumulated through observation, experimentation and reasoning. It reveals itself as a dynamic, evolving entity, intimately connected to the needs and commitment for those who pursue science. Familiar scientific developments frequently emerge and return suggesting different means of present-day thinking and science to develop. Speaking of, the word "science" roots from the Latin word *scientia*, and simply means "knowledge." First conceived in the 19th century, "science" and "scientist" are understood today. "Natural philosophy" was the term for study of the natural world and held a broader scope than modern science. For the sake of time-honored time and my own lack of knowledge, I will not bore the reader with the details of the evolution of natural philosophy and the science involving the interpretation of the natural world and human culture. Instead, over the next several issues of Links, the focus will include 1) the origins of the scientific revolution coinciding with the age of enlightenment, 2) the emergence of rationalization and 3) the role of France in the contributions to science and the relationship to the ISHLT.

Known as the early modern period, the beginning of the 16th century inspired thoughts of intellect and reason that led into the enlightenment, a time of scientific revolution. Scientists or rather Natural philosophers from Roger Bacon, Francis Bacon, Rene Descartes to Robert Boyle pioneered the way for new discoveries in the future. Like us, scientists, or rather natural philosophers of this era were familiar with the routine struggles and conflicts caused by politics and religion. For example, Giovanni Riccioli and Pierre Gassendi contradicted their political and dogmatic ideas to study genomics and optics. Along with these men, Nicolaus Copernicus tested the Catholic Church's principles to prove new scientific discoveries that challenged theories from over 1500 years.

Although Ptolemy had been known as the father of astronomy, Copernicus realized after carefully studying astronomy, that Ptolemy had made several errors with his research including the **geocentric** theory claiming the earth as the center of the universe. With heretical speculation, Copernicus tested the Ptolemaic system to establish that the sun is at the center of our solar system and the earth revolves around it while rotating on its axis. In 1513, Copernicus built his own solar system model. However, his observations led to some inaccurate conclusions including his assumption that planetary orbits occurred in perfect circles, as German astronomer Johannes Kepler would later prove planetary orbits are actually elliptical in shape, **eccentric** orbits. Copernicus's theories and research remained unpublished in his book *De revolutionibus orbium coelestium* until his dear friend and renowned mathematician Georg Rheticus published a treatise on trigonometry in Copernicus's name, which resulted in high success and promise for a good outcome. Before his death in 1543, Copernicus was finally able to see his discoveries in print and with little skepticism. That same year, Andreas Vesalius published his seminal works, *De humani corporis fabrica libri septem*,

as a major advance in anatomy, overshadowing the works of Galen which had been left unchecked for nearly 1400 years. Accordingly, 1543 marks the beginning of the Scientific Revolution.

Next, Galileo Galilei's support of **heliocentrism** and discussion of Ptolemaic and Copernican theories would, centuries later, result in house arrest and an unmarked grave. Unlike Copernicus, Galilei was viewed as heretical for lacking diction such as "if," which established his research as definite and elevated skepticism. In its many forms, science plays a key role in securing the success of future problems. Galilei's recognition of a failed major advancement in Copernicus and Ptolemy's works led to new concepts of instantaneous motion and gravitational theory. Although his theories on terrestrial motion were denounced due to ignited conflicts with the Roman Catholic Government and rejection of established ideas, his research provided enough conclusive evidence to overthrow past Aristotelian and Ptolemaic systems and explore new systems. Like infinite circles, Galilei dies in 1642 with stagnant research, the same year Sir Isaac Newton is born. Galilei's work led to help Newton in the development of dynamics and calculus.

The Enlightenment represents the importance of reasoning and self-awareness, and can be marked by Newton who authored the impressive book *Mathematical Principles of Natural Philosophy* published in 1687. Over time, the Royal Society in Britain established in the 17th century was losing its influence by the 18th century when the major focus of natural philosophy shifted to France. The major organizations of natural science were then disrupted by the French Revolution, shifting influence to the German states and their increasing roles in the natural sciences with a rise of an ideology of scholarship in German universities. In the 18th century, rational chemistry distinguished itself from alchemy resulting in the future of chemical explanation of periodicities, but I am getting ahead of myself.

Back to the matter at hand, attempts by natural philosophers in the 18th century examined natural laws with cues from astronomy according to Galileo, Copernicus and Kepler. These natural laws ruled the motions of the heavens culminating in the works of Newton. His reputation soared over time with support and promotion by [Voltaire](#). Discovery of natural laws replaced God as the explanation of why nature was as it was. Natural philosophers placed the operation of natural laws as the direct cause, such as the attraction of objections and motion. Theories of the earth were causal explanations of the earth's features. Instead of focusing on universal causal laws, a different approach emerged out of mineralogy in Germany because of the abundance of ore, metallurgy and mining in the Erz Mountains of Saxony. Practical interest on the location and properties of metals such as lead, copper and silver led German scholars away from the pursuit of universal causal laws. Rather than theory, they were more interested in empiric and practical observations. The primary German mineralogist of the late 18th century, Abraham Werner, emphasized careful observation and created a geological system based on the time of formation of rocks that proved enormously influential, especially on the Continent. Werner's work was an added voice to those who argued that the earth was a cosmic body whose past had been shaped by natural processes. Towards the end of the 18th century, he helped shaped the attitudes of thinkers with detailed attention to observation. Today, he is known as the father of German geology for having developed a systematic identification and classification of minerals. His work left an indelible mark on those who established geology as a science in the decades to come.

A sampling of these natural philosophers from different parts of the world over time were part of the scientific revolution that will eventually lead up to an amalgamation of rational thought and emergence of great scientific endeavors in France, which still influences us today in the ISHLT. These endeavors will be brought to life and remind us of the importance of history for our own personal enlightenment.

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