VINCENT'S NEW YEAR'S SENSE:

We ring in the New Year with reverie and resolutions as we prepare for further success in the ISHLT. We steer away from verbose blowhards with destitute and destruction into a serene horizon of tranquility. With a cabaret of fireworks from Christian Benden, we are given an update by the program committee as Adrian Lawrence takes us from "five easy pieces" to the seven principles for smart teaching. Then John Dark gently traverses Fitzgerald in the south of France. While Evan Kransdorf and Jignesh Patel sensitize our senses to heart failure and transplantation, Suneet Purohit and Natasha Altman break on through 2018 across another immune barrier. 2018 also brings the beginning of the end of yours truly's tenure as Editor-in-Chief of Links. Soon gone will be the days of the bombastic and bloviating platitudes and pablums all of you graciously put up with for the past seven years.

Happy New Year!

Vincent Valentine, MD
Links Editor-in-Chief

QUOTE OF THE MONTH:

"In literature the ambition of the novice is to acquire the literary language: the struggle of the adept is to get rid of it."

- George Bernard Shaw

WORD OF THE MONTH:

Bloviate –
To talk pompously; to talk at great length in a pompous and boastful manner.

IN THE SPOTLIGHT:

Program Committee Update December 2017

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I last reported as Program Chair just after my return from an extremely succesful Scientific Program Commitee Meeting in Chicago; it was the start of summer holidays in the Northern hemisphere. In the meantime, we have seen the first snow fall in Zurich where I live... But even more exciting things have happened, as the Scientific Program of our Society's 2018 Annual Meeting in Nice was produced and published online (available on the ISHLT website, www.ishlt.org, as FlipBook or PDF Brochure). Looking at the program content, I am very proud to report that the Scientific Program Commitee has done a tremendous job as a TEAM and is continuing to do so as we have just finalized the Abstract Sessions of the Annual Meeting.

For the ISHLT 38th Annual Meeting and Scientific Sessions to be held in Nice, France, from April 11th to 14th 2018, a record number of over 1800 scientific abstracts were submitted from all around the world. I was thrilled to watch that the vast majority of abstracts were submitted in the last 24 hours before the abstract deadline. Over 400 abstract reviewers subsequently peer-reviewed all abstracts, and I am very pleased to announce that 77% of abstracts were selected for oral presentations, mini-orals or posters, very well reflecting our Society's broad range of scientific expertise across the spectrum of advanced heart and lung disease. Further, the scientific content of the 2018 ISHLT Annual Meeting also mirrors our Society's diversity regarding disciplines, geography, gender and generations. Please note that general abstract acceptance/rejection notifications were sent out the latest by December 20th 2017.

As I mentioned in my last report, over two dozen Symposia and three Plenary Sessions are scheduled for the Annual Meeting in Nice. The three Plenary Sessions will be scheduled on Wednesday, Friday and Saturday, and Symposia throughout the meeting. Again we aimed to cluster program content. As with previous meetings outside North America, there will be no Sunrise Symposia scheduled in Nice.

I would like to take the opportunity to thank all Scientific Program Committee Members, the Abstract Selection Committee Members, all abstract reviewers and the extremely helpful and well organized ISHLT Staff for such great support. Everyone worked hand in hand, functioning smoothly and precisely like a Swiss watch.

In summary, I promise you an exciting Annual Meeting in Nice with a selection of the broadest possible range of high-quality research combined with great opportunities of networking in lovely

Nice. *The Acropolis Congress Center* located perfectly in the center of Nice provides the ideal surrounding for our Annual Meeting, also giving all attendees easy access to explore the beautiful city and to indulge in delicious food, particularly the "Cuisine Nissarde." There is no need to mention that Nice, the capital of the Côte d'Azur, at the Bay of Angels, is worth a visit.

Thus, now it is up to you to register for the 2018 ISHLT Annual Meeting (please remember the **Early Bird Registration Deadline** on February 22, 2018) to sort out your accommodations and to make travel arrangements. I invite you to also purchase tickets for our President's Gala Reception at the fabulos *Hotel Negresco* at the *Promenade des Anglais*, a stunning example of the Belle Époque in Nice.

Warmest Season Greetings and best wishes for 2018. See you all in Nice in April!

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

FOCUSING ON HEART FAILURE & TRANSPLANTATION:

Making Sense of Sensitization

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Introduction

Sensitization, the presence of circulating antibodies against human leukocyte antigens (HLA), affects approximately 25% of candidates on the heart transplant waiting list [1]. To reduce the risk of post-transplant complications including most importantly hyperacute rejection, antigens to which the candidate has strong antibodies must be excluded. This leads to a smaller potential donor pool, which in turn leads to an increase in waiting time and consequently a higher risk of adverse outcomes on the waiting list [1]. In this commentary, we address three important issues in the area of sensitization: 1) How do we measure the degree to which a candidate is sensitized? 2) What threshold should we use to define a candidate as sensitized? and 3) What should we do about sensitization?

How do we measure sensitization?

The *de facto* measure of sensitization has traditionally been the panel-reactive antibody (PRA) value. This value was originally derived using an assay that consisted of a panel of third-party T (for class I HLA antigens) or B (for class II HLA antigens) lymphocytes and the candidate's serum; the "PRA value" was equal to the number of cytotoxic reactions divided by the size of the "panel" x 100. Although there was no consensus about what PRA value defined a candidate as sensitized, most programs used a value of 10% [2]. This cell-based assay was subsequently replaced by an assay that measures antibodies against class I and class II HLA antigens using flow cytometry.

The next innovation in solid-phase methods was the use of Luminex technology that allowed a semi-quantitative assessment of the HLA specificities in a candidate's serum. For these methods, a new measure of sensitization had to be used as there was no longer any "panel." Zachary and Braun proposed a method that uses the gene frequencies of the excluded HLA [3] to predict the likelihood of a positive crossmatch. This method has been implemented by the United Network for Organ Sharing (UNOS), and the resulting value is known as the calculated panel-reactive antibody (CPRA). CPRA has been the official metric of sensitization for kidney transplant candidates since 2009 [4]. CPRA is exclusively a function of the HLA that are selected to be excluded.

CPRA as a metric of sensitization has both strengths and weaknesses. The major strength is that it summarizes the percentage of the potential donor population with HLA corresponding with the

candidate's HLA antibodies for both the class I and class II specificities as a single numeric value, which is therefore easy to interpret. In contrast, PRA reported values separately for class I and class II HLA antigens. Furthermore, CPRA can be further refined for HLA alleles, which are in the process of being added as potential excludes by UNOS.

However, CPRA has several important limitations. First and foremost, CPRA as implemented by UNOS does not currently include the frequencies for HLA-DQA1, -DPA1 and -DPB1 and thus is an incomplete metric of sensitization. Efforts are underway to correct this, and an expanded CPRA will likely be available within the next year or two. Inclusion of these loci is likely to result in higher CPRA values for candidates with these antigens [5]. Next, for very highly sensitized candidates, CPRA is not sufficiently granular to describe the level of sensitization [6], and the addition of decimal places is helpful. This also facilitates conversion of CPRA to its converse, the Likelihood of a Compatible Donor (LCD). LCD is equal to 1 - CPRA. LCD is a very useful metric for extremely sensitized candidates. For example, candidate "A" with a CPRA of 99% has a LCD of 1% or 1 in 100 donors, whereas candidate "B" with CPRA of 99.9% has a LCD of 0.1% or 1 in 1,000 donors. Thus, although these two candidates differ by only 0.9% CPRA, candidate "A" is 10-fold more likely to find a compatible donor. Furthermore, this concept of fold-change in compatible donors may be a promising way to look at the effect of desensitization [7].

What threshold should we use to define a candidate as sensitized?

It is important to reiterate that PRA and CPRA values are distinct. PRA is determined using beads that indicate which class I and class II HLA specificities are present in the candidate's serum, whereas CPRA is based on the HLA specificities above a certain mean fluorescence intensity (MFI) threshold that are present in the candidate's serum. The MFI threshold varies by HLA laboratory [8] and generally aims to correspond with the antibody strength likely to correlate with cytotoxicity; however, determining this value can be difficult and the concept of an MFI threshold is itself controversial [9]. Nevertheless, given that PRA is no longer the preferred metric of sensitization, the "over 10%" definition of a sensitized patient needs to reassessed.

We have recently used data from the UNOS database to show that CPRA is a continuous predictor of outcomes on the heart transplant waiting list [1]. At each successively higher level of sensitization, the number of candidates that were removed from the list or died increased, and the number of candidates who were transplanted decreased. As such, we would posit that the presence of any HLA antibodies defines a candidate as sensitized.

What should we do about sensitization?

Given that sensitized heart transplant candidates experience prolonged waiting times which in turn puts them at increased risk of decompensation before a transplant becomes available, several strategies can be utilized to improve outcomes for this population. First, careful consideration should be paid to selection of antigens to exclude. In addition to the Luminex single-antigen assay, our center utilizes dilution, C1q and complement-dependent cytotoxicity studies [10]. Next, desensitization with a variety of pharmacologic regimens can be implemented [11]. Desensitization has modest effects on CPRA, but as discussed above, any change in CPRA will result in a larger potential donor pool and thus increase access to transplantation.

Sensitization represents an important health disparity; most highly sensitized heart transplant candidates are women (67% of candidates with CPRA 80% to 100% are women, as compared to 20% of candidates with CPRA 0% to 20% [1]). Canada has implemented the "4S" (Category 4 for sensitized patients) system, which prioritizes organ allocation to sensitized patients based on their CPRA [12]. The 4S system was recently shown to effectively increase the size of the donor pool and improve transplant access for these very highly sensitized candidates. An allocation benefit for sensitization has existed in kidney transplantation in the United States since 1997. In 2014, the kidney allocation system was updated to provide an allocation benefit to sensitized candidates according to a sliding scale. A recent analysis has shown that this system has resulted in a significant increase in access to transplantation for extremely sensitized candidates [13].

In summary, sensitization is a common and important risk factor for adverse outcomes in heart transplant candidates and recipients. CPRA is the current best metric of sensitization and is undergoing updates, such as the ability to add decimal places, the use of LCD, calculation of CPRA based on HLA alleles and the addition of the HLA-DQA1, -DPA1 and -DPB1 loci. Further research is urgently needed to help improve access to transplant and to mitigate the immunology risk of these candidates.

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

References:

1. Kransdorf EP, Kittleson MM, Patel JK, Pando MJ, Steidley DE, Kobashigawa JA Calculated panel-reactive antibody predicts outcomes on the heart transplant waiting list. J Heart Lung Transplant; 2017;36(7):787–96.
2. Betkowski AS, Graff R, Chen JJ, Hauptman PJ Panel-reactive antibody screening practices prior to heart transplantation. J Heart Lung Transplant 2002;21(6):644–50.
3. Zachary AA, Braun WE Calculation of a predictive value for transplantation. Transplantation 1985;39(3):316–8.
4. Cecka JM Calculated PRA (CPRA): The new measure of sensitization for transplant candidates. Am J Transplant 2009;10(1):26–9.
5. Tinckam KJ, Liwski R, Pochinco D, et al. cPRA increases with DQA, DPA, and DPB unacceptable antigens in the Canadian cPRA calculator. Am J Transplant 2015;15(12):3194–201.
6. Kransdorf EP, Pando MJ Calculated panel reactive antibody with decimals: A refined metric of access to transplantation for highly sensitized candidates. Hum Immunol 2017;78(3):252–6.
7. Tremblay S, Shields A, Alloway R, et al. A prospective iterative trial of carfizomib-based desensitization trial: initial comparative observations. Am J Transplant 2017;17(S3):243–4.
8. Kamoun M, Phelan D, Noreen H, Marcus N, Klingman L, Gebel HM HLA compatibility assessment and management of highly sensitized patients under the new kidney allocation

system (KAS): A 2016 status report from twelve HLA laboratories across the U.S. Hum Immunol 2016:1–5.
9. Sullivan HC, Liwski RS, Bray RA, Gebel HM. The road to HLA antibody evaluation: do not rely on MFI. Am J Transplant 2017;17(6):1455–61.
10. Reinsmoen NL, Patel J, Mirocha J, et al. Optimizing transplantation of sensitized heart candidates using 4 antibody detection assays to prioritize the assignment of unacceptable antigens. J Heart Lung Transplant 2016;35(2):165–72.
11. Chih S, Patel J Desensitization strategies in adult heart transplantation—Will persistence pay off? J Heart Lung Transplant 2016:1–10.
12. Clarke B, Ducharme A, Giannetti N, et al. Multicenter evaluation of a national organ sharing policy for highly sensitized patients listed for heart transplantation in Canada. J Heart Lung Transplant 2017;36(5):491–8.
13. Stewart DE, Kucheryavaya AY, Klassen DK, Turgeon NA, Formica RN, Aeder MI. Changes in deceased donor kidney transplantation one year after KAS implementation. Am J Transplant 2016;16(6):1834–47.

FOCUSING ON JUNIOR FACULTY & TRAINEES:

Breaking Boundaries: Heart Transplantation in HIV-positive Recipients

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Even with advances in treatment, the long-term morbidity and mortality of heart failure remains high, and potential heart transplant recipients are becoming increasingly medically complex. Transplant centers are progressively treating heart failure patients not only for diabetes, hypertension and renal insufficiency, but also for chronic infectious comorbidities such as HIV and Hepatitis C. The prevalence of heart failure is significantly higher in HIV-infected patients than in non-HIV infected patients [1]. Current highly active antiretroviral therapy (HAART) regimens are able to suppress HIV viral loads to levels that enable patients to live longer with fewer side effects [2]. As a result, HIV is no longer considered a contraindication to heart transplantation [3]. However, cardiac transplantation is still infrequently performed in this patient population [4]. We present the case of a 53-year old male with HIV who recently underwent a cardiac transplant at our institution. The patient has given permission to share his case.

Our patient is a 53-year old male with history of New York Heart Association class IV systolic heart failure, monomorphic ventricular tachycardia status post biventricular ICD placement, HIV on HAART therapy, hypothyroidism and chronic kidney disease. Initially, he was referred to our institution from an outside facility due to progressive heart failure symptoms from multiple episodes of volume overload and ventricular tachycardia. He was diagnosed with HIV in 1995 in the setting of intravenous methamphetamine use. He was hospitalized in 2001 for pneumocystis pneumonia and cryptosporidium, whereupon he was started on HAART. He was managed at outside institutions for years and was referred for evaluation of his worsening heart failure. Upon our initial evaluation, he had been free of illicit drug use since 2001; HIV viral load had been undetectable for over 4 years, and his CD4 count was 429 on a HAART regimen of Viramune and Epzicom. After discussion with the infectious diseases team, the patient's HAART regimen was adjusted to abacavir/dolutegravir/lamivudine combination therapy for ease of use and to enable integrase inhibitor use. Protease inhibitors were avoided due to their interactions with calcineurin inhibitors. For multiple hospitalizations for volume overload and increasingly difficult to control ventricular tachycardia, he was listed and underwent successful cardiac transplantation in September 2017. His early post-transplant course has been smooth with no graft dysfunction and no evidence of significant cellular or antibody mediated rejection, which has enabled his prednisone to be tapered.

His HIV viral load remains undetectable and there have been no significant interactions with his HAART medications and immunosuppressant regimen of tacrolimus and mycophenolate mofetil.

Our patient's case demonstrates the resolvable challenges in transplanting HIV positive patients in an era of post-transplant immunosuppression and improving HAART therapies, employing a multidisciplinary team of cardiologists, infectious disease specialists and pharmacists. The use of integrase inhibitors such as raltegravir or dolutegravir have markedly decreased the risk of drug-drug interactions with immunosuppressants, since neither affect the CYP450 system which enables continuation of HAART therapy post-transplant [5]. Post-transplant antimicrobial prophylaxis for opportunistic infections is the same as for HIV and non-HIV infected patients as well. Data from other transplant centers show that while cardiac transplantation of HIV patients is still rare, 1 and 3-year survival rates are comparable to non-HIV infected patients [6]. The 2016 ISHLT guidelines have been updated to include transplantation of HIV positive patients as a Class IIa indication provided there is no evidence of active or prior opportunistic infection, CD4 count >200 cells/μl, and the HIV viral load remains undetectable > 3 months while compliant on HAART therapy [3].

Equipoise is one of the guiding principles in organ allocation networks. The limited data available on cardiac transplantation in HIV positive patients demonstrates that HIV infected patients derive the same benefit from heart transplants as non-HIV infected individuals with minimal difference in outcomes. Therefore, consideration of HIV-infected patients with well-controlled disease is reasonable enough to allow equal access to the scarce resource of cardiac transplantation.

Disclosure statement: The authors have no conflicts of interest to disclose.

References:

1. Kendall CE, Wong J, Taljaard M, et al. A cross-sectional, population-based study measuring comorbidity among people living with HIV in Ontario. BMC Public Health 2014; 14: 61.
2. van Sighem AI, Gras LA, Reiss P, Brinkman K, deWolf F; ATHENA national observational cohort study. Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals. AIDS 2010; 24 (10):1527-35.
3. Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. J Heart Lung Transplant. 2016; 35:1–23.
4. Uriel N, Nahumi N, Colombo PC, et al. Advanced heart failure in patients infected with human immunodeficiency virus: Is there equal access to care? J Heart Lung Transplant 2014; 33: 924–930.
5. Miro JM, Aguero F, Duclos-Vallee JC, et al. Infections in solid organ transplant HIV-infected patients. Clin Microbiol Infect. 2014; 20(7): 119-130.
6. Aguero F et al. An update on heart transplantation in human immunodeficiency virus-infected patients. Am J Transplant. 2016; 16 (1):21–8.

NEWS & ANNOUNCEMENTS:

Michael Kaye (1935-2017)

Michael Peter Kaye, surgeon, teacher, researcher, patriot and devout family man, died at the age of 82, on Sunday, Dec. 17, 2017. Born to Lithuanian immigrants, Mike was born and raised on Chicago's south side. Growing up with a strong interest in science, he studied chemistry at St. Louis University and went on to receive his medical degree from Loyola University's Strich School of Medicine.

During his residency at the University of Minnesota, he met Mary, his wife of 57 years, with whom he raised five children. Affectionately known to family as Harley, he shared his love of medicine, the outdoors, horses and the color gray with his children and grandchildren.

The family spent more than 10 years in Rochester where Dr. Kaye taught and conducted research related to heart transplantation at Mayo Medical School.

Dr. Kaye went on to serve as a professor at the University of Minnesota and UC San Diego, and was a key team member launching heart and lung transplantation programs at both institutions. He also was a founding member of the International Society for Heart and Lung Transplantation, where he established the transplant registry and was editor of the society's journal.

During his 40-year career, Dr. Kaye was committed to furthering the practice of medicine through teaching and research. A pioneer in heart and lung transplantation, he also led global efforts related to the collection, analysis and reporting of heart transplantation.

In addition to his transplant practice, Dr. Kaye proudly served his country at the USA Brooke Army Medical Center, Fort Sam Houston, Texas.

Dr. Kaye continues to teach in death. He donated his body to the Mayo medical school, where he will continue his studies with first-year medical students, as well as residents and fellows continuing their education.

Dr. Kaye is survived by wife, Mary; five children, Michael Jr. (Deb), Robert, Christopher (Andrea), Dory (Kirk) Anderson and Eric (Shawn); and 17 grandchildren and great-grandchildren.

To recognize Dr. Kay's dedication to medical education, the family requested donations be made to the Mayo Foundation for Medical Education and Research to support cardiovascular research.

SPECIAL INTEREST:

REVIEW: How Learning Works: Seven Research-Based Principles for Smart Teaching

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What does research say about how learning works? Where can a teacher find sound, instructional approaches to help students learn effectively and meaningfully? Is there a book that concisely explains and summarizes a philosophy of learning and yet provides practical strategies for real world application? *How Learning Works: Seven Research-based Principles of Smart Teaching*, by Ambrose et al, fits that bill. The authors and faculty drawn from Carnegie Mellon's Eberly Center for Teaching Excellence and the University of Pittsburgh set out to examine how students learn and how the principles of learning theory can be realistically applied. They manage to integrate research evidence drawn from the field of psychology, education, and cognitive science with practical experience for application in the college classroom. Note, this book was written with the college teacher and the undergraduate student in mind; however, those of us with a teaching or learning role within health professions will be well served by recommendations presented here. The strategies provided in most chapters can be applied easily to clinical teaching settings, simulation centers, and laboratory settings.

As implied in the title, *How Learning Works* is organized around seven inter-related learning principles that are paramount for learning success. In brief, the principles are: (1) prior knowledge, (2) organization, (3) motivation, (4) mastery, (5) practice and feedback, (6) development and climate, and (7) self-directed learning. Each principle forms a stand-alone chapter. The chapters are inter-connected but independent of one another, thus allowing for reading in any order. This is one of the book's key selling points for the busy clinical instructor who can read a chapter at a time without losing any understanding. All chapters share a common format. They begin with an attention grabber in the form of two typical classroom scenarios, which serve to introduce the principle at stake. This is followed by an in-depth discussion of the principle and ending with presentation of practical strategies for the classroom application. Contained within every chapter are tables and figures that summarize key "take home points." The final book chapter, another gem, provides ways an educator can use these learning principles to enhance their own lifelong learning. Eight appendices, found at the end of the book, provide very useful examples of learning objectives, student self-assessment, and other tools to complement the learning principles**.**

How Learning Works does an excellent job straddling theoretical and practical considerations. The book's comprehensive approach to effective teaching makes it an excellent resource for faculty who are interested in developing their teaching. Faculty who are in the early stages of their development will benefit from using these learning principles to frame their teaching. More experienced faculty, irrespective of their discipline or teaching style, will undoubtedly select a few

suggestions and integrate them into their teaching toolkit. All faculty will find that the seven learning principles are very useful categories of analysis when constructing course activities or reflecting on challenging learning situations.

In conclusion, *How Learning Works: Seven Research-Based Principles for Smart Teaching* provides deep insight to the theory and research of learning and offers concrete strategies to enhance teaching. The book's in-depth discussion of the seven learning principles lead the reader to a greater understanding of the learning process and the conditions that facilitate and hinder it. *How Learning Works* is an essential reading to discover research-supported practical strategies to help students learn effectively and meaningfully, irrespective of subject matter or environment. If you have a desire to improve your teaching and enhance learning, *How Learning Works: Seven Research-Based Principles for Smart Teaching*, would be a valuable addition to your library.

Book Review:
How Learning Works: Seven Research-Based Principles for Smart Teaching
Susan A. Ambrose, Michael W. Bridges, Michele DiPietro, Marsha C. Lovett, and Marie K. Norman, with a foreword by Richard E. Mayer. San Francisco: Jossey-Bass, 2010. ISBN-13: 978-0470484104. 336 pages, $40.00 US.

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Looking Forwards

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"North America gripped by Arctic Conditions," "UK set to be lashed by Storm Eleanor" are just two of the headlines (let's ignore politics) to greet the start of the year, with spectacular pictures of a frozen Niagara, metres of snow covering Pennsylvania and dominating avalanche warnings in the Alps. Looking back at 2017, described by a political observer, tongue in cheek as "an unexciting year," it is not only unrewarding, but rather bleak. So, let us look forwards, to some warmth and sun in 2018.

To defrost, the ISHLT will return to Nice in April with the warmth of southern Europe, the blue of the Mediterranean and the aromas of cheese and freshly baked bread. However, not just returning to Nice, but to France, a favourite of all countries- receiving more visitors than any other country in the world. It is centrally located in the western world (although the French would argue the whole world), and we should rejoice our return with the ease of travel.

Along with Louisiana, France gave us the metric system. The French Revolution gave us many ideals - *Liberté, égalité and fraternité*- behind "Western" democracies from New Zealand to Poland, although historically, we must overlook the guillotine, the Mob, Napoleon and his wars that devastated Europe for 20 years until Waterloo.

French writing holds a huge place – Camus, Sartre and Gide are just three of the record 15 winners of the Nobel Prize for Literature, more than any other country. Then there are the celebrated links with U.S. writers; we think of Hemingway in Paris with his contemporaries and F. Scott Fitzgerald, whose "Tender is the Night" has some of the most magical descriptions of the Cote d'Azur. He writes of the "diffused magic of the hot sweet South...the soft-pawed night and the ghostly wash of the Mediterranean far below."

The other obvious influence is in art – there are museums including Chagall and best of all, Matisse, in Nice itself, with Picasso and Renoir nearby. Music, film? I could give you many more examples of key personalities, but some contributions include *Lully to Satie*, *Renoir through Truffaut to Ozon* and *Bardot to Depardieu*. And, of course there was *Princess Grace*.

When looking at the field of medicine, there are still giants. Jean Dausset, Parisian immunologist, was one of the few who laid the foundation of tissue typing and received a Nobel Laureate in 1980 for his discovery of the HLA. The ISHLT Past President, Christian Cabrol, performed both the first heart and the first heart-lung transplants in Europe, the former 50 years ago. He died in the summer of 2017, and you can read a brief note in the July Links Newsletter, and a fuller appreciation by Jack Copeland in the *Journal of Heart and Lung Transplantation*.

Another star of French surgery was Rene Leriche, a mid-20th century man of huge talent. Every surgical trainee knows of the Leriche Syndrome– but also sobering insight. His famous quote "Every surgeon carries in himself a small cemetery, where from time to time he goes to pray" strikes a chord with all of us.

Others will write of the Annual Meeting – it promises to be one of the very best – and the specific delights of Nice. But come also to enjoy France. I end with two more quotes from F. Scott Fitzgerald:

> "*France has the only two things toward which we drift as we grow older - intelligence and good manners*."

And from "Tender is the Night," a novel rather more complex and every bit as good as "The Great Gatsby," when he writes again of the Mediterranean of an evening:

> *"...above a sea as mysteriously coloured as the agates and cornelians of childhood, green as green milk, blue as laundry water, wine dark."*

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