Vincent's Midsummer's English Sense

Since Paul Corris and John Dark have hit the mark for this issue and since I am on a well-deserved vacation (some of you will challenge this of course) I have very little sense to this add to this great issue. There is American English, Australian English, British English and Canadian English among many others. There is Standard English and nonstandard English. There is Old English, Middle English, New English, Archaic English, Colloquial English, Technical English and of course there is slang. There is Webster's Dictionary, Thorndike-Barnhart, American Heritage and of course there is the prize acquisition for any library, The Oxford English Dictionary (OED). The OED is now available online. It is a treasure-house for scholars, a go-to resource for all who study the history of language or literature. There is the *Corpus of Contemporary American English* and there is the *Corpus of Historical American English*. There are English speakers, English teachers, there are lexicographers and there are linguists.

There are 6000 languages spoken in the world today. English has borrowed from not quite all these languages. But there are more people on Earth who use English as their secondary language than there are those who use English as a primary language. If we are going to better understand what people say or mean and if we are going to improve our communication then we must all have a better command of the English language to understand the subtleties and dialects and make fewer mistakes.

The English language is impure—it is an amalgam of many borrowed words developed from contact with different cultures, colonization, regionalization, imperialism and now globalization. It is a melting pot which will continue to brew and stew into a richness that will never be fully cooked or complete. If the only thing or concept that remains constant is change, then the English language unceasingly changes. Some of us may believe these changes represent erosion, while some of us may believe these changes are continual refinements. These changes have been considered mistakes or errors, but we should be reminded that there is no success without failure. Either way the English language is essential to communication, and I am quite certain the English language is unquestionably a word hoarder.

I leave you with this, Shakespeare had no dictionary.

And as an open invitation, any member of the Society is welcome to submit to the *Links Newsletter* any editorial comments on the proper—and improper—use of the English language, and why, so that we might improve communication with our colleagues, our patients, and one another.

Vincent Valentine, MD
Editor-in-Chief, ISHLT *Links* Newsletter

In the Spotlight: 100 Days and Counting

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It is a galling and enlightening reality that 100 days have already passed since assuming the role of President of this wonderful Society. So much to do and so little time! Vincent has asked me to provide a few thoughts on these busy days so I trust you will find what follows of interest. There have been three phases:

Recovery and Reflection

The ISHLT Annual Scientific Meeting in Montreal provided the culmination of the year spent as Program Chair and more than fulfilled expectations. Not only were the excellent venue and city itself a delight, the meeting content and activity was of the highest order. Many sessions were standing room only and the palpable excitement of the attendees an ever present reminder of why face to face meetings will always serve our membership in a way that cannot be superseded by other means. Some rest, reflection and internalization of lessons learned are a necessary sequel to such an event but from a personal perspective had to be brief due to the assumption of Presidential duties!

Team Building

Having worked on the Board for the last 4 years, the mechanics of the Society are no longer a mystery and as previously stated the machine room, run so well by our Executive Officers, provides clear direction in matters of protocol and corporate memory. The new Board provides a blend of experience and vitality and I look forward with great enthusiasm to a productive year. A clear balance of sectional interests has been achieved to foster a true international flavor to deliberations on matters of importance. Already a number of key issues have been discussed at the July Board teleconference and await final action including the Society's response to developments in international organ donation policy and practice as well as our relationship with the fledgling International Right Heart Failure Foundation where we will have two representatives on the Nomenclature Committee.

The Way Ahead

So what lies ahead? Planning for the 2014 San Diego Annual Scientific Meeting is well underway and the Program Committee Meeting, under the able chairmanship of Jason Christie, met mid-July in Philadelphia where the Committee crafted a fascinating assortment of hot topics into an educational extravaganza. Wait till you see it! I am sure you will be impressed. Start planning now to submit abstracts and to attend. Remember in 2014 the meeting will run from Thursday thru Sunday and include some extraordinary and exemplary plenary speakers.

In closing, it is my abiding pleasure to serve in this role and I commend to all the manifold benefits of the Society membership augmented by participation keeping us out of the dark and in the spotlight.

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

The Bacchanal Buzz of Antibodies in Heart Transplantation

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At the 2013 ISHLT meeting in Montreal, the Heart Failure and Transplant Scientific Council chose to have members submit citations with a brief synopsis of interesting articles published in journals outside ISHLT. Below are my evaluations of three citations which might be of interest to heart failure and transplant medicine specialists. In addition, Howard Eisen contributed a report for this issue entitled, mTOR Inhibition: Where We Have Been, Where We Are, And Where We (Hopefully) Will Be Going, which you don't want to miss.

Citation: Role of anti-vimentin antibodies in allograft rejection, Rose ML, Human Immunology (2013), doi. Comments by Dr. David Nelson based on unedited manuscript accepted for publication.

Synopsis: Marlene Rose's excellent review of anti-vimentin antibodies (AVA) in this issue provided the following points:

1. AVA probably results from tissue damage coupled with inflammation.
2. Rejection injury is a prerequisite for AVA acceleration of rejection.
3. The mechanism of AVA acceleration or accentuation of rejection may include the proinflammatory effects of complement fixation and pro-thrombotic effects of platelet activation.
4. AVA are not inhibited by CyA but are more suppressed by mycophenolate than azathioprine.
5. AVA may be associated with cardiac graft vasculopathy.
6. Higher AVA titers occur in recipients of non-heart-beating long-ischemic-time kidneys than heart-beating short-ischemic-time kidneys.
7. One study showed renal transplants with pre-transplant AVA IgG had higher incidence of chronic graft vasculopathy.
8. Prolonged dialysis may increase AVA.
9. Unpublished study by Rose ML and Smith JD found AVA IgM in 10% and 6%, respectively, of 350 heart and 458 lung candidates (pretransplant). AVA IgG was not measured.
10. Rose cites Nath et al's study in this journal (Journal of Heart and Lung Transplant 77:1604-1609, 2004) as demonstrating an association between AMR and AVA.

Citation: Vimentin antibody production in transplant patients and immunomodulatory effects of vimentin *in-vitro*, Carter V and Howell W. M. Comments by Dr. David Nelson based on unedited manuscript accepted for publication.

Synopsis: Vaughan Carter and W. Martin Howell compared AVA levels in end-stage heart, lung, kidney, and liver patients to 100 blood donors and found that AVA were mostly IgM and mostly found in end-stage liver patients and kidney re-transplant candidates. Primary biliary cirrhosis was the major AVA risk in the liver group, and HLA DQ2 was the AVA predictor in the failing kidney graft group. Primary biliary cirrhosis is an autoimmune disease and DQ2 is associated with autoimmune diseases such as SLE and celiac disease. Some of the renal transplant patients were biopsy C4d positive with negative HLA DSA and responded to plasma exchange.

Citation: Banff Initiative for Quality Assurance in Transplantation, (BIFQUIT): Reproducibility of C4d Immunohistochemistry in Kidney Allografts, Mengel, et. al., American Journal of Transplantation 2013; 13:1235-1245, comments by Dr. David Nelson.

Synopsis: In 2009 the Banff initiative for quality assurance in transplantation (BIFQIT) was developed to assess and improve reproducibility of C4d immunohistochemistry (IHC) reported in kidney transplantation. The first BIFQIT trial was published recently by Mengal et al in the American Journal of Transplantation, 2013; 13:1235-1245. Unstained slides were sent to 73 institutions for staining by local protocols and interpretation and then returned to a central panel for re-interpretation. The results showed that:

1. There was poor inter-institutional reproducibility (Kappa 0.17).
2. The institutional variability was equally due to inter-observer (Kappa 0.44) and inter-laboratory (Kappa 0.46) limitations.
3. The central panel read higher scores than local labs, which the authors suspected was the result of local pathologists adjusting their scores to their local clinical experience.
4. False positives were uncommon.
5. The study suggested that simplification of histologic grading would improve reproducibility. Reproducibility was best with C4d negative and strongly positive slides. Intermediate grades were where the most variability occurred.
6. Four specific recommendations for tissue staining and processing were provided (table 4 of the article).
7. The authors note that alternative criteria for renal AMR is being evaluated in recognition of reported C4d negative AMR.

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

mTOR Inhibition: Where We Have Been, Where We Are, And Where We (Hopefully) Will Be Going

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You may be surprised to see my smiling face once again gracing the Links and are no doubt wondering "is this guy going to be a regular feature of this otherwise "hot" august Newsletter?" Before you decide to change websites, specialties or perhaps even careers, let me reassure you that I am writing this column by special invitation of (and of course provided with an extension by) David Nelson, HF and TX MED Council Communications Liaison, so take up your complaints with him. But before you do, there is a method to his madness which is that he has requested that I discuss the role of mTOR inhibitors (or PSIs) in cardiac transplantation with commentary on the recent clinical trial of everolimus in the *American Journal of Transplantation* (1) as well as the accompanying editorial written by Mandeep Mehra, who was moonlighting from his regular job as Editor-in-Chief of the *Journal of Heart and Lung Transplantation* (2) and another article about everolimus by Masetti in the very same issue (3). Given the opportunity to expound and pontificate with my sanctimonious platitudes as well as to respond to the editorial about my article, how could I resist? Let me also say that I do undertake this article with some trepidation as Mandeep is my Editor and I fear being tossed off the Editorial Board or worse, being relegated to reviewing only case reports. But that wouldn't happen, right Mandeep, buddy (right Mandeep?)?

Why are we interested in developing and evaluating new immunosuppressive agents? Why would 63 transplant centers on five continents join forces to conduct a clinical trial of a new immunosuppressive agent in 721 patients if there was broad contentment and satisfaction with the current state of immunosuppression? As expertly stated by Mandeep in his Editorial, "the real Achilles heel is late attrition with an 11-year median cardiac allograft survival" and among the reasons he cites are cardiac allograft vasculopathy (CAV) and cancers (2,4). In fact, these two complications have remained the major causes of mortality beyond the first year post-transplant despite the overwhelming switch to mycophenolate mofetil (MMF) over a decade ago. If we ever want to be able to tackle these problems so that we can provide our patients with the assurance that they will have long lives and get the best longevity from the scarce resource which is the transplanted heart, we need new immunosuppressive agents and new strategies.

It was with this in mind that two clinical trials, one comparing sirolimus to azathioprine, the other comparing everolimus to azathioprine, demonstrated less biopsy proven ISHLT Grade 3A (2R) rejection and less progression of CAV (5,6). All IVUS measures of CAV showed less progression with the mTOR inhibitors but the focus was on one measure in particular, change in maximal intimal thickness from the baseline to one year post-transplant IVUS which had previously been shown to have prognostic significance for survival and major adverse cardiac events (7-9).

Limitations of these studies included the elevated creatinines with the full-dose cyclosporine regimen and the fact that MMF has long since supplanted azathioprine as the preponderant anti-proliferative used clinically.

It was with the goal of addressing these issues that the everolimus trial published in the AJT was conducted, specifically using MMF as the comparator and using reduced dose cyclosporine, which had been shown in the earlier study to provide similar protection against rejection in the presence of therapeutic doses of everolimus. The same two doses of everolimus (1.5 mg and 3.0 mg daily) studied in the earlier trial were also included in this one. Against MMF, which is more potent than azathioprine, everolimus was non-inferior for the composite endpoint, which included biopsy proven ISHLT Grade 2R rejection. Additionally renal function in the everolimus group, expressed as mean eGFR from MDRD, was significantly decreased compared to MMF (59.5 vs. 64.7 ml/min/1.73 m2, p=0.009 at month 12 and 59.5 vs. 64.5, p=0.020 at month 24). The potential reduction in nephrotoxicity from using the combination of PSIs and CNIs was predicated on adhering to the defined reduce dose cyclosporine regimen in the everolimus arm which was quite different from the standard of care regimen used in the MMF arm and in cardiac transplantation in general (at my own center, my highly skilled and experienced transplant coordinators threatened to call psychiatry and/or the police when I adjusted cyclosporine doses according to the study protocol in the everolimus group). But the results of the study highlight the importance of what my teachers in elementary, junior and senior high school said which was "pay attention" (all except the French teachers who said *"faites attention"*). Of the 63 centers, ten did not achieve the separation in cyclosporine exposure between the two groups (they did not pay attention or were intimidated when their coordinators threatened to call the police). If one looks only at the 53 centers that did adhere to reduced cyclosporine protocol, there was no significant difference in eGFR at 12 months compared to MMF.

Mortality with everolimus was an issue and the 3.0 mg dose arm was discontinued early by the DSMB. The 1.5 mg arm was also associated with numerically more deaths than MMF at 12 months (22 vs. 13 respectively) but by 24 months this difference had narrowed (30 vs. 25 respectively). Interestingly, 17 deaths occurred in the everolimus 1.5 mg group within the first three months post-transplant (compared to 5 in the MMF group) and a majority of these from infection in patients who received induction with ATG. The trifecta of ATG induction, LVAD as bridge to transplant and everolimus increased the risk of death from infection. In the non-induction and basiliximab groups, these differences were not seen. The observation that over-immunosuppression leads to infection and that nothing good can come from it is not new but was observed in prior studies such as the Daclizumab trial (10).

Adverse events were noted in the everolimus groups, specifically more pericardial effusions which often needed to be drained and this would represent a side effect for which the clinician would need to be vigilant in the earlier post-transplant period. The withdrawal rate was in the 30% range in the everolimus group, higher than that observed in the MMF group but lower than the 40% withdrawal rate reported in the original MMF vs. azathioprine study (11).

Once again, patients receiving everolimus had less progression of CAV as defined by a variety of IVUS parameters and this was true in a number of high-risk patients such as diabetics. The incidence of IVUS-defined CAV was a very low 12.5% in the everolimus group compared to 26.7% with MMF. As Mandeep mentioned in his Editorial, the IVUS population was different from the general study population demographically including percent Caucasian (less in the IVUS group) and percent receiving induction therapy (more in the IVUS group); mean creatinine was numerically but not statistically different between the two groups (IVUS 1.33 mg/dl vs. 1.42 for non-IVUS). IVUS is a highly specialized technique, which requires considerable expertise both in its performance and interpretation, which is why (along with lack of insurance reimbursement) it is largely relegated to clinical trials. Coronary angiography is universally available and less complex to perform and analyze which is why it was made the cornerstone of the ISHLT CAV guidelines (12). As with IVUS, its use would be limited by abnormal renal function and its utility in predicting future adverse events is only now being defined. Clearly for either IVUS or coronary angiography, the ability to predict mortality and other major adverse cardiac events would be essential and needs to be evaluated in the context of clinical trials.

It is always good when a study's findings are reproduced and Masetti's study also shows that everolimus, when initiated in the early post-transplant period, appeared to attenuate the progression of CAV: when started late (after one year), this attenuation was not seen (3). There are important differences between this study and the clinical trial mentioned above. Masetti and colleagues performed an observational, non-randomized study of patients in their clinical practice and the number of patients was small. Their observations for the effect of everolimus on IVUS defined progression of CAV is similar but their results cast doubt on the utility of everolimus to mitigate established CAV: further prospective studies will be required to address this issue. They too had no information regarding the utility of IVUS to predict future adverse events.

What to make of this long ramble and what is the bottom line? Everolimus has a narrow therapeutic index as Mandeep indicated but so do the CNIs. If used correctly, one can mitigate the renal insufficiency seen with concomitant full dose CNI but one has to adhere to a markedly different CNI regimen. There are drugs that should be avoided if one is going to use everolimus de novo, specifically induction with ATG. There are patients who should be avoided, specifically those with infected VADs. There is the opportunity for reduced progression of CAV as defined by IVUS and this was also shown by Masetti's study. Whether this translates into fewer major adverse cardiac events in the future is not known and can only be extrapolated from prior IVUS studies. Longer-term follow-up of the patients in both of these studies might answer this question. These drugs may provide the hope of preventing or mitigating CAV; the trade-off is adjusting to a new, more complex post-transplant immunosuppressive regimen.

Disclosure statement: The author reports that he received grant support to conduct the clinical trial described above and that he was a member of the study's Steering Committee. This research support has concluded. The author wishes to thank Dr. David Nelson for the opportunity to once again monopolize the ISHLT Links and to have his picture plastered on that same Newsletter. He also would like to thank those who have allowed him once again to have an extension but this is

really becoming a habit. As indicated above, the author is an FOM (Friend of Mandeep). He and Dr. Mehra plan to take this show on the road. You can catch their next performance at the ISHLT in San Diego in April 2014 (unless they get booked in Las Vegas, Atlantic City or by David Letterman or Jimmy Fallon before that).

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PRE-ANNOUNCEMENT: Donor Management Research Consensus Conference

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The Health Resources and Services Administration (HRSA) will host a Consensus Conference on September 16 and 17, 2013, at the Sheraton, Pentagon City, in the Washington, D.C., area. Multiple issues related to the core issues of donor consent, recipient consent, and possible development of a national IRB-like oversight panel will be explored. HRSA anticipates an attendance of approximately 120. Registration cost is anticipated to be approximately $150. The clinical stakeholders driving the development of this Consensus Conference are AOPO members and ASTS abdominal surgeons. Thoracic transplantation has been less involved.

This Consensus Conference will lay the foundation for what eventually may determine how you, your institution, and your patients will be informed about donor intervention trials and frame your obligations to your institution and patients regarding this information.

HRSA will announce the conference to stakeholders when conference planning is further along. There is an article recently published in the *American Journal of Transplantation* titled "Challenges to Research and Innovation to Optimize Decreased Donor Organ Quality and Quantity" which provides a good four-page exposure to the issues of interest to the Consensus Conference. When you see the formal HRSA announcement of this Consensus Conference, I strongly urge you to consider attending.

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Spreading the Word on the ISHLT Working Formulation for Cardiac AMR

Dylan V Miller, MD
Chair, ISHLT Pathology Council

Gerald J Berry, MD
Pathology Program Committee Member

Much of the Pathology Council's efforts in recent years have focused on standardizing the diagnostic criteria for antibody-mediated rejection (AMR) in cardiac transplant biopsies. These efforts have been fruitful in terms of finding agreement between pathologists at many centers around the globe as well as coordinating closely with clinical colleagues in revising the Working Formulation for AMR.

Still, pathology faces a unique challenge within the ISHLT relative to our colleagues in other specialties. During the "day-to-day" work at our home institutions, reading transplant biopsies occupies only a tiny fraction of our time. Most of us wear many other hats and spend the bulk of our time far removed from transplant pathology on surgical pathology, autopsy, or other pathology services. The Pathology Council members' involvement with the ISHLT stems from our passion for this work and dedication to these patients. Membership and attendance at the annual meeting is a luxury many practicing pathologists who sign out your heart transplant biopsies literally cannot afford. We know this in part because only 47 ISHLT members are pathologists (according to member profile data), while the ISHLT registry data indicate 394 transplant centers worldwide and 241 currently reporting. Just ask yourself, do the pathologists reading my biopsies attend ISHLT? Chances are, the answer will be no. At most centers, transplant biopsies are read by a pathologist who is not a member of ISHLT.

So, the challenge for those of us on the pathology council, besides encouraging recruitment and greater participation from our pathologist colleagues, is ensuring that the "water gets down the furrows in the field" when it comes to the Working Formulation revisions. We realize it is time to stop preaching to the converted and start taking the message abroad.

To that end, we have submitted a new manuscript to the *Journal for Heart and Lung Transplantation* intended as an exhaustive atlas or monograph type reference to aid pathologists in applying the Working Formulation for Cardiac AMR in biopsy interpretation. It includes numerous illustrations that highlight important histologic and immunopathologic features of AMR from several cases contributed by the authors. Besides further descriptive summaries of criteria for diagnosing AMR, there is also a discussion of controversies and knowledge gaps that deserve further investigation (like what to do with focal C4d staining, how many macrophages is too many, and integrating DSA and clinical signs into the diagnosis of AMR).

Members of the Pathology Council have also collaborated with the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology to help develop an Online Tutorial for grading cellular rejection in cardiac transplant biopsies. An accompanying tutorial for AMR is under development as well and several members of the Pathology Council are participating. These tutorials will be an invaluable resource, not only for pathologists and pathology trainees, but for clinicians, surgeons, nurse coordinators, and anyone else needing an introduction or even "refresher" to the Working Formulation grading scheme for cardiac rejection. The tutorials even include live viewable slides (digital whole slide images) for teaching.

Members of the Pathology Council will also be presenting a CME course at the major annual pathology society meeting (United States and Canadian Academy of Pathology, 2014) next year, focusing on heart and lung transplant biopsy pathology and the revised Working Formulation.

All of these resources will be available to all pathologists regardless of membership in ISHLT. Our ultimate aim is to improve adherence to the revised Working Formulation criteria worldwide, but this is also a public relations campaign of sorts that we hope will encourage greater pathologist participation in ISHLT.

The heart is just the start; efforts are currently underway to better define the diagnostic features of AMR in lung transplant biopsies. As Dr. Gerry Berry states, pulmonary AMR continues to be a vibrant topic of special interest to the Pathology Council. Following up on the success of the pre-meeting in Prague in 2012, a group of thoracic pathologists met in Montreal on Tuesday, April 23, 2013 to further refine diagnostic criteria. A series of cases of AMR were presented and the histopathologic findings and immunophenotypic profiles were each evaluated and discussed to develop diagnostic thresholds for interpretation. Dr. Roden of the Mayo Clinic presented their experience of concurrent IF and IHC staining for C4d on a series of transbronchial biopsy specimens. Further refinement of the morphologic constituents of pulmonary AMR will be the goal of both future meetings and studies.

The coming year in the Pathology Council promises to be exciting and productive as we continue to contribute and refine the histopathologic criteria for grading of rejection in a deliberate and evidence-based manner. We look forward to a vigorous interaction with our clinical colleagues in the Society to meet these goals, and we also hope that our clinical colleagues will help recruit new members to the Pathology Council from Pathology Departments in their medical centers in order to better disseminate and standardize these diagnostic criteria.

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

Transplant Greats: Talking with Sharon Hunt

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At the Junior Faculty and Trainee Council meeting, we decided to introduce a series of features on the legends in the field of heart and lung transplantation to try and catch a glimpse into the lives of these inspiring individuals and to get to know them beyond their bibliography. This is our inaugural feature.

Transplant Greats – Talking with Sharon Hunt

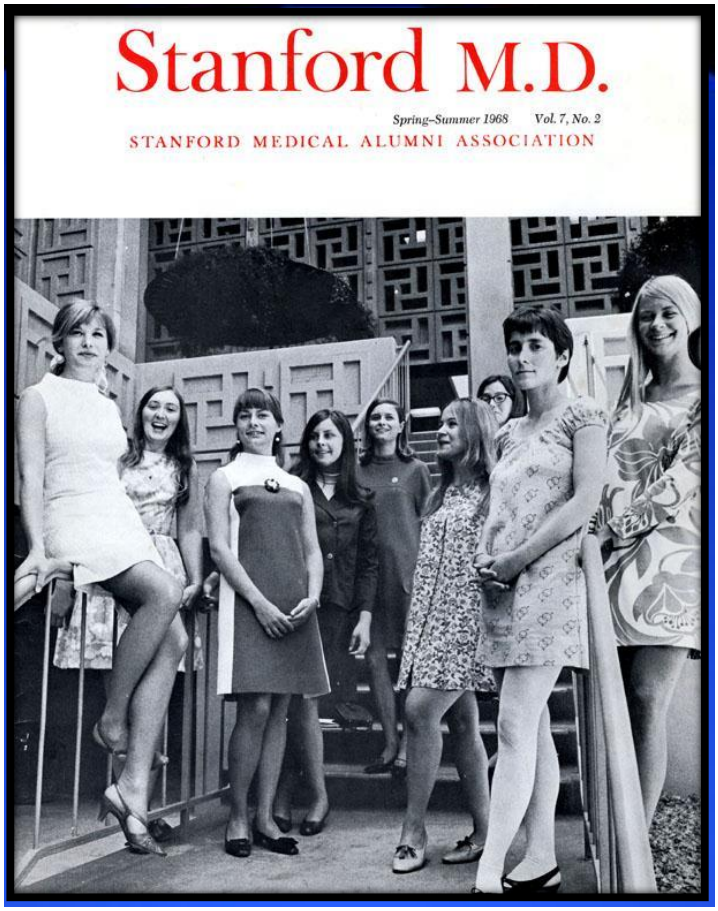
As an ISHLT 2012 Lifetime Achievement Awardee (a title amongst numerous others bestowed upon her over the years), Sharon needs no introduction to the readers of the ISHLT Links Newsletter. Born and brought up near Cleveland, Ohio, to an engineer father and a homemaker mother, she recognized science as an early passion. In her early years at an all-girls catholic school, she developed a 'healthy distaste for nuns', but distinctly remembers a certain charismatic nun – her biology teacher. She fostered in Sharon a keen interest in botany and spurred her on to study photosynthesis and plant physiology as an undergraduate at The University of Dayton in Ohio. And then she discovered something 'so much more exciting than photosynthesis' – the Department of Artificial Organs at the Cleveland Clinic. Under the tutelage of Dr. William Kolff and Dr. Irvin Page, Sharon was introduced to the life of medicine and there has been no looking back.

Sharon was featured on the front page of the Spring-Summer 1968 edition of the *Stanford MD* (the Stanford Medical Alumni Association) – the first year Stanford Medical School had more than one woman student in every class. Also featured in that same issue was the first adult heart transplant performed in the US by Norman Shumway marking a major cardiac transplant milestone. These two featured articles brought forth the conception of our matriarch in heart transplantation.

The following year, more than 100 transplants were performed, with an abysmal survival of less than 30%. The surgery was almost abandoned as a viable option but for the efforts of Norman Shumway and his team. Around this time, he enrolled Sharon's help with the post-transplant care of his patients and their academic partnership bore path-breaking results that redefined the science of heart transplantation. She fondly remembers him as a dynamic personality with a righteous sense of humor who never hesitated in narrating a 'dirty joke' if it fit the occasion. Shortly following the initial success of surgeries, *Life* magazine featured an article on how patients 'went crazy' post-transplant and questioned the viability of this procedure. It did not take Sharon long to figure out that these patients were having their vital signs checked every hour, effectively denying them any sleep! They changed their nursing patterns allowing for patients to get sufficient rest, and the issue all but resolved completely.

So what keeps Sharon going? In her own words, "practicing transplant cardiology keeps me honest and it definitely never gets boring." Between her outstanding academic and clinical career, she has learned the fine art of managing a four acre farm in Santa Cruz, although she is still trying to figure out how to keep the deer at bay! In addition to being the quintessential role model for every transplant cardiologist, she is a devoted mother, an equestrienne, adventurer, traveler and a Dr. House fan. She strongly encourages female cardiology fellows to consider transplant cardiology as a career choice and firmly believes that it does not discriminate against women but *vice versa*.

Her advice to young faculty? Learn when and how to say no and make wise choices to suit the quality of life you want for yourself.



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

Dr Hunt was the 2012 recipient of the ISHLT Lifetime Achievement Award. Read more about this at http://www.ishlt.org/ContentDocuments/2012MayLinks_Lifetime.html.

NEW!! International Fellowship Database

Manreet Kanwar
ISHLT JFTC Vice Chair

The Junior Faculty and Training Council is proud to announce an **International Fellowship Database** which was created with the goal of disseminating information and improving visibility of highly specialized fellowships in the field of heart and lung transplant. Based on survey responses provided by ISHLT members, we have collected information on international training opportunities in adult and pediatric heart failure, heart and lung transplant, mechanical circulatory devices and pulmonary hypertension. This is not a comprehensive list and ISHLT does not endorse the programs listed or information provided in this database. For more information, visit the Junior Faculty & Trainee Council Webpage.

Letter from Across the Pond

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July is ending on a high note despite the continued faltering economy. We have enjoyed glorious summer weather and continued international sporting success. Not only was the Lions tour of Australia (Rugby Union) a triumph, the first XI cricket team is trouncing their Australian opponents at the time of writing. Thirdly, Froome C has just won the coveted Tour de France without resorting to foul play (trust me I'm clean). Fourthly we rejoiced at Murray A's triumph at Wimbledon, at least all save those who have been unable to forgive him for his support of anybody but England jibe during an interview as a fresh faced Scottish teenager. Most recently, Hamilton L won the Hungarian F1 Grand Prix and Farah M sprinted clear of the field at the "Remember the Olympic Games" anniversary meet over a distance that he would generally consider too short to run. Capping it all, the new Royal Prince finally arrived to the relief of the world's press, not to mention the Duke and Duchess of Cambridge. Public opinion suggests a degree of satisfaction within the country not felt for some time.

Alas, there is one area for which turbulent storms continue to gather momentum within the very structure of what we hold most dear. The very fabric of our beloved National Health Service is slowly being unraveled by reorganisation as new commissioning plans unfurl and scandals regarding patient care rock its very foundations to the core. As former Health secretary Alan Johnson said recently "The next stage [of the reorganisation of the NHS] began with I believe Lord Ara Darzi's review, a great clinician, a colorectal surgeon, who came in and led from the bottom up."

Bottom up is the current worry indeed.

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George Alexander Louis and the Press

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"It was summer" was the excuse, "a quiet news day".

Is that really the best explanation of media hysteria, almost everywhere in the world? Or are we seeing yet another example of what Christopher Hitchens described as the "cretinism of royal coverage"? (Waving? Or drowning?)

At home in the UK, even the left wing, previously republican (and we are not talking GOP) *Guardian* newspaper devoted most of the front page and four more inside—a day's work for half a dozen reporters. At least their headline, "A Birth, A Boy, A Prince, A King," something a future Kenneth Branagh might declaim with Shakespearean gravity, was better than the almost uniform "It's a Boy!" from the tabloids.

But big news in all the US outlets, the Canadians lit up the Parliament building in blue, and from my vacation viewpoint it's all over the French press. Here, serious broadsheets such as *Le Parisien* managed to cover large areas of the front page. "Everything you want to know about this birth" is the translation of their banner headline. Maybe the French are envious of a monarchy, having disposed (sharply, do we hear the Editor pun?) of their own a mite over 200 years ago? The past two presidents in this blessed and colourful country show the clear disadvantages of having ceremonial and political leadership vested in one person.

To add to a world view, the Iranian government sent good wishes. However, Teheran state TV described the Queen as an iron-fisted dictator using the birth to distract the downtrodden populace from massive austerity. Perhaps they were confusing her with the late Margaret Thatcher?

Back in the UK, the monarchy is as popular as ever. This continues to defy reason; they cost a lot, have essentially no useful political role and there is the lingering suspicion that, with the undoubted exception of the current monarch, they aren't very smart. Centuries of interbreeding amongst and between the royal houses of Europe must have done some harm! All of the royal family perpetuates the myth of un-earned privilege.

But there is a role as a focus for the national identity; witness, although now a year ago, the Olympic opening ceremony. It does seem that they do this better than any elected alternative, at least for a medium sized European country, as my comments about French presidents illustrate.

So we are stuck with the Royals, certainly for my lifetime!

The problem remains of what to do with the Press, and the Media, as a whole. Hitchens described the "mental habits of royalism" but this now goes for the whole of our brittle celebrity culture. To quote Hitchens again, he wrote, more than a decade ago, of how royal coverage operated "with the intensity of Gresham's Law", the bad driving out the good and "encouraging laziness and sentimentality and salacity by making it too easy to fill page upon page with brainless twaddle."

This now describes the great swathe of our news media. If as a newspaper, you have to compete by volume (has anybody weighed the *New York Times*, or any of the British Sunday papers recently?), then quality goes out of the window. The same goes for TV and radio; if you have to operate rolling 24 hour news, most will be repetitious and most will be junk!

So it's not the fault of the Royals, for all their deficiencies. If there is the same story everywhere in the world, blame the media. Page after page of the same, in all honesty, trivial story is just an illustration of their laziness—and our lack of discrimination!

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Laughing Links

Dan Dilling

Bob Mankoff is the cartoon editor for The New Yorker, who is featured in an upcoming short film about New Yorker cartoons called Very Semi-Serious. For this month's Laughing Links feature, we encourage you to watch a recent TED talk by Mr. Mankoff. It is really funny, even if a bit long at 21 minutes. In it he describes the process and philosophy behind writing and choosing the famous New Yorker cartoons and even gets into the essence of humor. And he picks some of his favorites to highlight his points! Enjoy! Bob Mankoff: Anatomy of a New Yorker Cartoon

Word of the Month

"wittol"

noun Archaic.
a man who knows of and tolerates his wife's infidelity.

Editor's Corner:
Telling Dildrams and Talking Whiff-Whaff

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Regional speech has always been a source of fascination and survives via collections of traditional stories, folk songs, poetry and dialect based translations of well-known literary works. In a country like the United Kingdom which has been conquered and held by foreigners of several different nations during its early history, it follows as a matter of course that that a great variety of dialects will be found to prevail in different parts of the Kingdom. The languages that can be found to influence local dialects include Ancient British, Roman, Danish, Saxon and Norman.

One of the characteristics of many dialects is that the same word or at least a word that is pronounced in the same way may have more than one meaning and this is very important to realise when engaging in conversation with a person versed in dialect.

"Good Morning and how are you feeling today?" Im very adle today, Doctor. Any the wiser? Well adle is a corruption of the Saxon word adel meaning disease. The derived word addled indicates a swollen state due to pus or corrupt matter. To describe oneself as "very adle" indicates a strong feeling of malaise and weakness. Easy then. Well not quite because in contrast the verb ***to addle*** also indicates the act of rewarding for labour completed as in ***"to addle his shoon"*** which indicates the feeding of a working horse with a good volume of oats and in rural parts describes the said horse's antics in rolling from side to side on its back in anticipation of a good feed. Addle indicates a feeling of satisfaction then and whilst variation in the inflection and emphasis of syllables and of course context may provide further clues to the meaning of words with more than one, it is quite possible to misinterpret what is being meant. Of course, our silver-tongued Editor (an American with a southern dialect behind his American English) might sarcastically respond, ***I'm not unwell, thank you*** or more likely, ***I'm good*** or ***I feel good***.

A ***"canny lass,"*** for example, can indicate that the female person you are describing is shrewd, frugal with money, good, lucky or pretty depending on intonation and context. ***Yaping about*** and ***swabbling like a trubagully*** may sound like a serious neurological disorder until one realises that it simply describes the general activity of basic chat from a person who is employed in a rather menial occupation.

Patients then may choose to use words to try and convey how they feel which leave us uncertain as to what is being said. The problem may lie in unfamiliarity with the word itself or choice of a word with more than one meaning. Remember the conversation between Humpty Dumpty and Alice in Lewis Carroll's *Through the Looking Glass* (1872):

"When I use a word," Humpty Dumpty said, in rather a scornful tone, "it means just what I choose it to mean—neither more nor less."

"The question is," said Alice, "whether you can make words mean so many different things."

The reality, Alice, is that many words do have differing meanings.

History taking remains the corner stone of diagnosis and careful analysis of the language a patient uses when describing symptoms is vital to prevent the potential for misunderstanding. Whilst the correct interpretation of dialect is particularly relevant when practice involves patients from diverse regions, it is equally important to clarify exactly what a patient is trying to tell you when using words in common usage. Remember Humpty Dumpty who chooses a word to mean to what he chooses it to mean. Time spent clarifying what the patient means exactly (and do please remember clarify means both making clear and easier to understand or removing impurities or solid matter as in butter) is generally a more direct and cost effective approach to achieving a correct diagnosis than reaching for multiple investigation request forms in the hope of elucidating what is going on.

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