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## WE'RE EXPANDING OUR *Links* EDITORIAL BOARD!

We are currently looking for 3-4 more members to expand the editorial board of the ISHLT LINKS Newsletter. Interested members, especially those who can provide an international perspective on issues of interest to the ISHLT community are requested to submit a short CV to the Editor, David S. Feldman, M.D. at [dfeldman@mplsheart.com](mailto:dfeldman@mplsheart.com), with a copy to Susie Newton at [susie.newton@ishlt.org](mailto:susie.newton@ishlt.org) by **February 15, 2011**.

# ISHLT *Links*

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## THE "TEST": Just take it!

James B.Young, M.D.

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On November 3, 2010 many of my good friends, colleagues, partners, and mentees trekked to an automated commercial "test center," were imprisoned for about 10 hours, and subjected to an assessment of their knowledge base for a professional qualification (FIGURE). The "test" became the talk of this year's American Heart Association Scientific Sessions held in Chicago a few days later - well, at least in my circle.

The trekkers were wide ranged in age, stature, position and experience, but they had all had one thing in common that morning – to experience, take, and pass the American Board of Internal Medicine (ABIM) Subspecialty Certification Exam for Advanced Heart Failure and Transplant Cardiology. You should know that I wasn't amongst that brave group of pioneers (more on that later). But I did participate in the exam post mortem with both test makers (don't worry, they are all sworn to secrecy and gave away nothing of value) and test takers (who ranged from being blasé to highly agitated and irritated with every stage between). The test makers were an interesting and eclectic group of senior statesman in the field with impressive academic and clinical credentials.

Though not formally taking this particular exam in a formal session, they were required to participate in the "ABIM exam experience" with some taking the Cardiovascular Disease Subspecialty Recertification examination. The test takers, for the most part, thought the exam a bit rough with some ambiguities, grueling, but generally fair. Many pointed out that there were numerous seemingly picky points about, for example, some clinical

trials that are in our lexicon. Others noted that, for the most part, the direction of questions focused on consensus, the professional society guidelines, and a core knowledge base that most well trained board certified cardiologists should already have (hemodynamics as an example). Virtually everyone, and, arguably, all of the more mature test takers (meaning their hair is as grey as mine) commented unfavorably on the cost of the test (\$2,785) and the rather uncomfortable Gestapo like environment found at the test centers. The older generation of our heart failure mafia is not used to that sort of test taking because we are "grandfathers and grandmothers" and not required to recertify subspecialty distinction by formal examination – it is assumed that our passion for the profession and continuing medical education will keep our knowledge base and skills up to snuff (something, perhaps, we should readdress).

Yes, I am unnerved by the descriptions of the testing process (and confirmed by a review of the ABIM web site instructions) (1); arrive with multiple identifications (at least one with a photo and signature), allow your palm and finger prints to be taken (I don't think they do iris scans – yet), remove your watch, wallet, key ring, mobile phone, pager, Black berry or other PDA, lock them up and strip naked for a body cavity search (alright, not yet anyway – I am being facetious). At least if you need your nitroglycerine or bronchodilator you can take that in with you (well, as long as it is identified as "essential" and you have received prior approval from ABIM – see the web site). What about aspirin for that headache you are going to get straining to read a computer screen all day?



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And then there was the videotaping that was going on. For me it is sad that all of these draconian steps must be taken to ensure the integrity of the examination. It is an affront to scholarship! Perhaps knowing that was the standard operating procedure is what dissuaded me from taking the test (more on that later). I suppose it should be comforting knowing that “irregular behavior” will be reported by the “test administrator,” and that sophisticated “forensic techniques that use statistical analysis of test-response data to identify test fraud, including cheating and copyright infringement” are also used (1). But it is not. For my experience, just give me a room of empty tables with a lot of space between bodies, a really mean looking proctor marching around, numbered test books and bubble-in answer sheets, and a LOT of #2 (only) pencils with HUGE erasers (I used to make a lot of changes on these tests). The good ‘ole days? Some would argue that we’ve come a long way from the legendary inquisition format of “oral” exams that many specialties and subspecialties administered (and still do on occasion today). Those examinations were apparently tainted by examiner conflict of interest and inequality of testing, according to some test takers of yesteryear. So why would hardy and hale self anointed Heart Failure and Cardiac Transplantation specialists subject them to such an experience? That question is actually easy to answer, in my opinion – pursuing the passion of scholarship and academics and putting our patients first is the answer. Put differently, becoming the first to be officially certified as an Advanced Heart Failure and Transplant Cardiologist and qualifying for a new, distinct and, likely, privileged guild. Kudos to them.

Some say the definition of a specialist is an individual who knows more and more about less and less. But is the parsing of cardiology good? Is specialization and sub specialization helpful to our patients? Is it something a cohort of likeminded folk should pursue? Are there rewards and benefits to the process and outcome? Who will end up quarterbacking, in a general care sense, our patients with cardiovascular disease if everyone sub-specializes? Certainly medical specialization has been around for eons and this evolution of specialization is inevitable.

Think of the trade guilds of the renaissance, for example – specifically the barber surgeons. One can visit Barber-Surgeons Hall in Monkwell Square, London, where it has been located since 1430, and view the incredible Hans Holbein portrait of Henry VIII (well, a copy) and

then pop over to the Royal College of Surgeons to visit the Hunterian Anatomic Collection, representing the profession more as we now know it, having split away from the Barbers (or “sub-specialized”) in the mid-1700’s. Indeed, the Royal College of Surgeons is a guild of sorts. Today, guilds are still quite important and have continued to evolve with the times. Just think of the Boilermakers and Teamsters Unions and even the ABIM. So to my point, the profession of Medicine gave birth to the specialty of Internal Medicine, which spawned Cardiology, which begat Electrophysiology, Imaging, Cardiac Rehabilitation, Cardiac Imaging, Nuclear Cardiology, and now Advanced Heart Failure and Cardiac Transplantation. Characteristics of these modern day guilds include a narrowed focus of interest, a common and commonly understood knowledge base that is deep rather than broad, a curriculum, programs designed to teach those interested and qualified to learn, a focused professional society, regular scientific conclaves, a body of enduring materials and, usually, a dedicated professional journal, with external recognition that a bona fide “specialty” has emerged and exists. This is generally accomplished by a professional guild governing body, such as the ABIM, creating and administering an examination to objectively demonstrate an individual’s mastery of a specific knowledge and skill base. Subsequently accolades are usually distributed by yet another professional society such as the American College of Cardiology.

These characteristics usually, at least in the medical profession, lead to credentialing criteria and standards, reimbursement adjustments, and public or professional (often times academic) recognition. And so “taking the test” will, de facto, legitimize recognition of the newly emerged specialty field of Advance Heart Failure and Transplant Cardiology; a sub-specialty of Cardiovascular Disease and sub-sub-specialty of Internal Medicine. Mastery of the examination will document mastery of the field, at least for the moment, and legitimize this new guild. So just “take the test!”

How did we get to this point? I have listened while many luminaries have discussed this issue and related entertaining tales of progress in our specialty. For me the emergence of the field really began in the 1970’s shortly after Barnard pressed everyone forward with his first “successful” heart transplant. A new knowledge base was required and a new focus on heart failure and cardiac transplant medicine began. Of course it is ludicrous to ignore the brilliant work done earlier to describe cardiopulmonary physiology and cardiovascular



disease. After all, this body of work defined the normal and abnormal cardiovascular physiology that was essential for describing, in a modern day sense, “heart failure.”

Focused research began in congenital heart disease, hypertension, atherosclerosis, myocardial infarction and cardiac ischemia, arrhythmias, and heart failure. As more attention was paid to heart failure, per se, individuals began devoting their entire research and clinical career to heart failure and cardiac transplant medicine. Devoted clinics were created and grew, albeit haltingly, in the early 1980's. Lots of patients were flowing into these efforts and many saw patient and programmatic benefits. Heart transplant centers emerged. The United Network of Organ Sharing (UNOS) developed criteria to become a “heart transplant physician,” and Medicare demanded a credentialing, of sorts, for transplant physicians and surgeons.

Major medical meetings like those of the American Heart Association and the American College of Cardiology began devoting large blocks of time to the subjects of heart failure and cardiac transplantation (and later to mechanical circulatory support devices). Cardiovascular trainees realized the research and clinical opportunities in this arena were robust. Nascent groups such as the Cardiac Transplant Research Database (CTRD) group led originally by Dr. Leslie Miller and then by Drs. James Kirklin, Robert Bourge and David Naftel at the University of Alabama, Birmingham, brought together like-minded individuals interested in and focused on heart failure and heart transplant. Meetings held during the AHA became legendary for their social and scientific events. The Heart Failure Society of America emerged as a dominant force in the field complete with a journal and annual meeting. The International Society of Heart and Lung Transplantation continued a focused mission evident in the name of the society.

Subsequently, several additional professional journals emerged that focused on the topic. Particularly important was that in 1995 The American College of Cardiology published the COCATS Guidelines for “Training in Adult Cardiovascular Medicine” and for the first time set the curriculum for “Training in Heart Failure and Transplantation” (2). This was an effort led by Dr. Sharon Hunt and designed primarily to advise programs on how to train individuals to meet criteria developed by the UNOS to become a cardiac transplant physician, necessary to support a “Medicare” or, now, CMS, certified heart transplant program. These training guidelines were revised in 2002 (COCATS II) and then again in

2008 (COCATS III) (3, 4). Advanced fellowship training programs created with some frequency, and hospitals, group practices, and academic medical centers searched for, and hired cardiologists with special expertise in heart failure and cardiac transplantation. There is certainly job security in this field with the mounting burden of advanced heart failure in North America! It was then in the context of leadership discussions within the Heart Failure Society of America and American College of Cardiology, primarily, that a strategy was developed for approaching the ABIM with a request to consider creation of a certification examination for Advanced Heart Failure and Transplant Cardiology. Arguably, the main reason for doing that was to confer legitimacy on the new “specialty” we all felt existed and were passionate about. Clearly, linked to the reasons specialties develop and evolve in the first place there were many other reasons to pursue this designation.

It was not that the group desired narcissistic recognition for their professional efforts. A finely choreographed dance then began in 2007 as the COCATS III curriculum, to be released in 2008, for advanced fellowship training in “Heart Failure” was created. I was been fortunate enough to be on the 1994 and 2002 COCATS and COCATS II writing committees chaired by Dr. Sharon Hunt and had the honor of being asked to Chair the 2007 effort along with committee members William T. Abraham, Robert C. Bourge, Marvin A. Konstam (sitting president of the Heart Failure Society of America), and Lynne Warner Stevenson. An entirely new curriculum had to be developed and focused on Level I or general “core” training, Level II or “intensified experience” training, and Level III or “advanced training in heart failure.”

Dr. Mariell Jessup became an ad hoc, albeit unrecognized, member of that committee as she was an important leader in both HFSA and ABIM. She served as a critical, bright, tactful and energetic bridge between ABIM, HFSA and ACC. We were proud of the COCATS III curriculum that was developed because, with the support of ACC and HFSA (lead by Dr. Konstam at the time), and based on the explicit definition of “advanced heart failure training,” ABIM ultimately agreed to recognize Advanced Heart Failure and Transplant Cardiology as a sub-sub specialty of Internal Medicine. This story is clearly truncated here, with very few seminal names mentioned. Hopefully, a more detailed history with appropriate and scholarly attributions with luminary recognition will appear one day. But, another reason to “take the test” is to affirm the time consuming and hard work of our leadership and



thank them!

Finally, to give additional reasons for “taking the test” we should return to the issue of specialization evolution and, more generally, progress in our profession. As was alluded to above, in the end it is all about scholarship. Ernest Boyer, a past President of the Carnegie Foundation for the Advancement of Teaching, education guru, and fire starter, preached about the four essential support beams of scholarship being discovery, dissemination, application and teaching (5). This is, indeed, exactly what happened with our specialty and now marked by ABIM ratification. To me it is also affirmation that scholarship is NOT declining in medical education, at least in the arena of advanced heart failure, as some have argued (6). Certainly research and clinical experience primarily drive insight and practice, but it is scholarship that defines the specialty and that, ultimately, is why some sort of competency assessment or “test” is mandatory.

Unfortunately, the “testing” approach is superbly flawed, perhaps best evidenced by the draconian requirements for actually taking the test and reviewed. We must look at alternative ways to judge achievement of competency and, more importantly, we must create an atmosphere of lifelong scholarship that is reliant on self-directed learning, critical thinking, and problem-solving, with a passion for the profession, professionalism, and ethics. Evidence of attainment of competencies that define the specialty should be based on data developed and demonstrated over time that is held in a personal and professional “portfolio” that is much like an artist’s or architect’s portfolio. Both formative and summative evidence based portfolios should become the norm. Not “tests,” particularly not tests that require a strip search! Younger trainees and other professionals desiring later-in-life specialty certification should be charged with developing a portfolio of evidence that is properly reviewed that, perhaps, includes reflective essays highlighting areas of strengths and pointing out targeted areas for improvement. Clearly defined ways to achieve and assess competencies mandated by the COCATS III training curriculum can and should now be developed. That would be the real “test.” But for now we are stuck without that – so just “take the test.”

And so November 8, 2010 will become an iconographic date for some in our profession as it represented true recognition and legitimization of the specialty of Advanced Heart Failure and Transplant Cardiology. So just “take the test.”

So for me, why didn’t I take the test? That question is for another essay – so in the meantime, do as I say, not as I do. Yes, I have been the parent of many teenagers!

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## An American Dilemma

David Feldman M.D.

The question to submit to our readers is, “does the current American System benefit all of the heart failure patients in the year 2011?” An alternative way of looking at this same concern is, “do we need to reconsider what are the eligibility criteria for a heart transplant?”

The most recent data set would suggest that more than 50 percent of all heart failure (HF) patients have diastolic heart failure. The majority of these patients are women. Some of these patients will develop end-stage HF, but our current listing system makes it difficult to list these patients for transplant with preserved left ventricular function. Many other groups of patients are also disadvantaged by our current system including those with isolated or predominate right sided heart failure, hypertrophic cardiomyopathies, some valvular cardiomyopathies, as well as some congenital or familial heart patients. Alternatively, some patients are uniquely advantaged by a system which is out of pace with our current understanding of heart failure epidemiology. Specifically, should stable ventricular assist device (VAD) patients be afforded an automatic one month of IA time when one-year survival data exceeds 90 percent? Should we be more rigid about what a life threatening infection in a VAD patient means? That is, does a drive-line infection constitute a patient right to be IA, without regard to how will this impact other patients?

In short, the current UNOS allocation system needs to be re-visited. It is not likely that more donor organs will be available in the next decade, yet the number of HF patients will almost certainly increase in an exponential fashion. Some data may suggest that we will be seeing less patients with cardiomyopathies caused by coronary artery disease and more patients with cardiomyopathies resulting from untreated hypertension, diabetes or the conditions listed above. Although assessment of maximal VO<sub>2</sub>, NYHA class and ejection fraction have been determining who should be listed, the weight we give to each of these can be regionally and individually unique to a given medical center or region. We can no longer count on whether a patient looks “good” to determine when they should be listed or not listed. Perhaps all our system needs is a little more finesse and guidance. Although we all agree that no one

“number” should determine if a patient should be listed, some insurance companies are not as open-minded.

Our current complacency and water cooler discussions are not helping to change our system so that all of our patients with a similar risk of dying have an equal chance of being transplanted. We need to re-address how we are allocating a scarce resource. In the next issue of ISHLT Links, our British and German colleagues will present how their allocation systems deal with these difficult questions.

Finally, we would also like to invite our readers to submit their comments (to be published in the next Links issue). Change happens with adversity and a desire for people to evoke change. Now is the time to reopen the discussion on whether we need to revisit how we allocate hearts to our patients on the waiting list.

We all know there are variances in how patients are treated by different medical systems. Are patients with end-stage HF dying because they don't fit in a traditional category? Are patients dying on the list because others are supplanting them inappropriately based on current outcomes data? Regrettably, there may even be some gaming of the current system, which may further skew outcomes and disadvantage some patients. So the question remains, “do we need to revisit our current system?”



## Questions that Matter: The Search for Trials in Cardiac Transplantation

David Baran, M.D.

Cardiology is one of the strongest bastions of evidence-based medicine, with an enormous number of trials having been conducted in the last 20 years, addressing many of the common problems in the field. Much of this work has been funded by industry (usually pharmaceutical or device manufacturers). In addition, funding from the National Institutes of Health and allied governmental sources has led to a rich database of diseases such as ischemic heart disease and stroke. There are numerous drugs under development at this time, and therefore many trials in progress or in planning.

In the realm of cardiac transplantation, the situation is decidedly different. Research in the area of cardiac transplantation peaked in the two decades following the introduction of cyclosporine and later tacrolimus. Many trials elucidated the role of tacrolimus versus cyclosporine, and then interest turned to substitutes for azathioprine, leading to trials involving mycophenolate mofetil, sirolimus, and everolimus. There were trials of induction drugs such as daclizumab, and basiliximab, although most of these involved a relatively small numbers of patients.

The decade beginning with 2010 has been marked by the loss of patent protection for most of the commonly used drugs in our field, and thus the economic reality that “Big Pharma” will no longer be able to make large investments in randomized trials to answer the pressing questions which arise. Cyclosporine, mycophenolate mofetil, tacrolimus, sirolimus, azathioprine and corticosteroids are all generic, and therefore not likely to be the subject of industry funded trials. Despite a large investment in a well designed clinical trial, daclizumab is no longer available worldwide, leaving basiliximab which has a much more limited dataset in heart transplant patients.

The National Institutes of Health is funding a program of research in solid organ transplantation, known as Clinical Trials in Organ Transplantation (<https://www.ctotstudies.org>). The first of the trials in heart transplant was an observational trial but a new trial is beginning to examine the role of rituximab in non-sensitized patients undergoing transplantation. While this is an interesting trial, it did not arise from a common clinical problem.

In my opinion, it is time for the heart transplant community to decide what the pressing questions are, and then lobby for funding to answer these in order of priority. What follows is my own personal view and is meant to stimulate discussion and debate.

To appropriately set priorities, it is necessary to focus on a goal, and traditionally transplant medicine has focused on allograft rejection. I would submit that we have fought that battle and emerged largely victorious. Most reports indicate that allograft rejection occurs in a minority of patients and is rarely fatal.

The battle should shift to amelioration of morbidities which are largely caused by the medications that we prescribe for our patients. Some problems, such as malignancies, are more challenging to study prospectively given the relatively late onset and low frequency of such disorders. On the other hand, problems such as side effects of steroids or anti-proliferative drugs (mycophenolate mofetil or sirolimus) are more common, and affect a broader number of patients.

In particular, steroids are the class of drugs we “love to hate” with many programs declaring that patients are aggressively weaned from steroids by one year post-transplant. However, the ISHLT registry data continues to show that more than 50 percent of patients continue to receive corticosteroids at five years post-transplant. It is not plausible to think that more than half of patients worldwide are classified as “frequent rejectors” where their clinical status drives lifelong use of corticosteroids. Certainly, there are problems with discontinuing corticosteroids after one year post-transplant. There are concerns about adrenal insufficiency, which could be unmasked by removal of steroid supplementation. In addition, clinicians logically are concerned about disturbing the delicate balance between the patient’s immune system and the graft, and worry that late rejection will accompany discontinuation of steroids.

On the other hand, there is no evidence that corticosteroids are particularly essential in the modern framework of immunosuppression, especially with calcineurin antagonists like tacrolimus. In liver



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transplantation, corticosteroids are usually discontinued rapidly, and immunosuppression monotherapy with tacrolimus alone is an accepted standard of care in some centers. There are several reports of renal transplantation in combination with very minimal doses of corticosteroids, typically in patients receiving induction antibody treatment.

These reports have not led to a groundswell of support for minimization of immunosuppression in heart transplant patients. It seems that many of us in transplantation regard our chosen organ (whether it is heart, kidney or liver) as “special” and therefore we don’t heed the lessons learned in other organ models, especially if the other organ is below the diaphragm! The cardiac literature does support the utility and feasibility of reduced immunosuppression, with several reports of successful steroid weaning dating back to the early 1990’s, as well as retrospective reports of tacrolimus monotherapy in cardiac transplant recipients. The prospective Tacrolimus in Combination, Tacrolimus Alone Compared (TICTAC) trial enrolled 150 patients, and showed comparable outcomes for patients randomized to tacrolimus and mycophenolate mofetil versus tacrolimus monotherapy in heart transplant recipients, all of whom were rapidly weaned from steroid therapy.

A prospective, randomized trial of rapid steroid weaning versus a more conventional pace of steroid withdrawal would have enormous practical implications for patients

worldwide, but faces large obstacles. Perhaps the most significant problem will be the lack of an industry funding source, given the generic status of most of the immunosuppressants in common use. Hopefully, other sources of funding will be obtained so that we can answer the question of the role of steroids (after more than 40 years of ubiquitous use in transplantation).

There doesn’t appear to be an agent “on the horizon” that will match the impact of the calcineurin inhibitor drug class, and thus research in the foreseeable future needs to be directed to making the most of our current pharmaceutical tools. As a community, we should insist on evidence based-trials of drug strategies to allow better decisions to be made for our patients. In turn, we have to be ready to adopt the results of the trials, as is the standard in cardiology in general. If we find that patients do equally well with less medications, for example, then we need to “let go” of the teachings of our past and adopt new ideas in the best interest of our patients. We may find that the heart, while special and magical, is not so different than the liver and kidney after all, and that ideas from “below the diaphragm” hold relevance to our patients and practice. Only by embracing evidence based transplant medicine will we move our field forward.



## Heart and Lung Transplantation in Israel

Tuvia Ben Gal, M.D.

Inspired by the pioneering works of Norman Shumway and Christian Barnard, Morris Levi from Beilinson Medical Center in Petah Tikva performed the first heart transplants in Israel, and the 100th heart transplanted worldwide in December 1968. Similar to experience in other centers at that time, the 42-year-old recipient survived for only a couple of weeks and died of infectious complication. After the failure of the second heart transplant two months later, the public in Israel doubted the moral appropriateness of the operation and the program was closed.

The modern cardiac transplant programs in Israel started in August 1987 when Josef Borman performed a heart transplant at Hadassah Medical Center in the holy city of Jerusalem. In 1992, Dan Aravot and colleagues and Jacob Lavie and colleagues performed heart transplants at Beilinson Petah Tikva and in Sheba Ramat Gan Medical Centers respectively.

The first lung transplantation was performed by Josef Borman in 1992 at Hadassah and the first heart and lung transplant was performed a year later at that same medical center by Gideon Marin and colleagues.

Since the beginning of chest organ transplantations, 250 hearts, 200 lungs and 11 heart and lung transplants were performed at the three transplant centers.

Due to the worsening scarcity of organ donors, the number of heart transplant performed per year has been gradually declining with the recent average of 20 heart transplants performed per year nationwide.

Approximately 70 percent of heart transplant recipients in Israel suffer from ischemic cardiomyopathy.

The centrally funded National Center for Organ Transplants is the organization responsible for the national organ allocation with representatives in all the hospitals in the country identifying potential organ donors. Once a donor is identified and determined to be acceptable, his/her clinical characteristics are presented to the representative of the national center responsible for patient data. An allocation is recommended based on the blood group and donor size, with transplant candidates hospitalized due to intractable heart failure having the highest priority. If a clear priority between two potential recipients hospitalized at two of the three transplanting centers is not apparent, the cardiologist from the third

center is asked to make a determination of priority. In the rare cases when there is no matching high urgency patient, the longest waiting patient of the approximately 130 patients on the national waiting list is selected.

It is estimated that about 20 percent of all patients on the waiting list and as many as 50 percent of the high urgency patients die while awaiting a suitable organ. The high rate of death while awaiting heart transplantation resulting from the severe organ shortage affects many aspects of the medical care of those patients: approximately three to eight patients per year are sent abroad for heart transplantation and the number of patients bridged to heart transplantation with ventricular assist device is expected to outgrow the number of transplants performed, imposing a high economic burden and some new moral questions we have not faced before.

Organs for lung transplant candidates are allocated according to the Lung Allocation Score.

Our law mandates consent for organ donation by the closest relatives. One of the main obstacles for the initiation of the transplantation programs in Israel came from the religious parties. The approval of the procedure by the religious authorities, resulting from a very long and tedious process, opened the door for the first transplants performed by Josef Borman in Jerusalem. Nowadays, beside some very extremely orthodox Jewish and Islamic groups, there is no religious official objection for organ donation.

Organ donation in Israel was found to be unaffected by the ongoing political conflict: organ donation rates among Arabs and Jews are proportional to their representation in Israel's general population as well as to the ethnicity of the patients on the national heart transplantation waiting list.

The Israel Transplantation Society, the Israel Heart Society and the national committee for the prevention of cardiac and vascular diseases proposed extended criteria for the acceptable heart donor targeted at maximizing the use of hearts recovered from the potential donors in Israel. These criteria were accepted in order to overcome the worsening donated organ shortage and increase the number of patients saved, but the tradeoff for that increased number of donors might be reduced survival,



an issue to be studied in the years to come.

After favorable experience with the HeartMate II ventricular assist device and its approval for destination therapy, four centers in Israel were selected to perform implants: the three actively transplanting centers and Carmel Medical Center in the northern city of Haifa. Approval was given for twelve devices per year to be used nationwide as destination therapy. The total number of LVAD's implanted in Israel is gradually increasing with 20 implants expected this year.

Organ transplantation in general and heart transplantation in particular has been the window through which people contemplate the medical expertise of the different medical services extrapolating the transplantation success to the medical quality of that center. A successful organ transplantation program demands a multi-disciplinary cooperation. In Israel, all the hospitals in the country are funded to manage organ donors, and therefore this

cooperation is also multi-center.

Considering heart transplantation in Israel, peace and equality have been achieved: proportionately equal numbers of Jewish and Arab organs are donated and those organs are transplanted to the same proportion of recipients from both ethnic groups.

Although the ongoing religiously based conflict in Israel is far from ending, medicine, organ transplantation and in particular heart transplantation with all the emotional connotations related to that organ, might be the one area that brings Jews and Arabs together to save the lives of their loved ones and make some real progress towards bringing our hearts closer politically by mixing them medically.

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## Heart and Lung Transplantation in Norway 1983 – 2010

### Oslo University Hospital - Rikshospitalet

Oslo University Hospital, Rikshospitalet, Oslo, Norway is the national center for heart (HTx) and lung transplantation (LTx) in Norway (4.9 million inhabitants).

The first HTx was performed on November 6, 1983 and was also the first in Scandinavia, the first heart-lung transplant (HLTx) was performed in 1986, also the first in Scandinavia. The first child had HTx in 1984. The first single lung transplant (SLTx) was performed in March 1990, and the first bilateral sequential lung transplant (BLTx) a year later.

There are 28 registered donor hospitals in Norway. Presumed consent is acknowledged by the law, however the family is always consulted. 85 percent of the donors are domestic, the rest are from the ScandiTransplant organ exchange program. Donor age has increased from 27 years to 37 years in the last five years. 60 percent of the donors are males. Mean ischemic time has increased slowly and is now close to 160 minutes.

Since the inception of the HTx program, 755 HTx have been performed in 737 recipients, of whom 44 were individuals younger than 17 years of age, with the youngest recipient being one-year-old. On average, 28 HTx have been performed each year since 1983. After 2000, between 30 and 35 HTx have been performed annually

with an all time high in 2003 resulting in 45 HTx (10/million inhabitants/year). In a 2008 European Council Newsletter, Norway was credited as the leading HTx country worldwide, with 7.7 million HTx inhabitants per year. In contrast to international trends we have not experienced the reduction in donor availability and decreased numbers of HTx during recent years. The waiting list is relatively short, consisting of 10 to 15 candidates with an average waiting time of  $3.7 \pm 1.6$  months. In the last 10 years we have had a five percent death rate while waiting for HTx.

All HTx candidates are evaluated by our team at our hospital. Guidelines as published by Mehra et al. (JHLT 2008) are used for listing of HTx candidates. After listing, the patients are seen every third month or more often if necessary. As the only center offering circulatory support we admit all critically ill patients in our hospital for mechanical circulatory assist (MCS). Overall, one percent of the patients have been supported to HTx by ECMO, IABP or LVAD, but the use of MCS has been increasing and since 2005, 25 percent of the patients received circulatory support as bridge to HTx. Our implantable LVAD program started in 2005 (VentrAssist and later HeartWare) and 28 LVADs have so far been inserted (age 10-69 years). Three patients are currently



being supported, four died, one recovered and 20 were successfully bridged to HTx. One patient has HeartWare BIVAD and is awaiting HTx as an outpatient. Average time on LVAD support has been  $208 \pm 116$  days. The longest LVAD treatment has been three and a half years and is still ongoing, an HTx is not being pursued by patients choice due to good quality of life .

In adults, coronary heart disease is the leading cause for HTx (47 percent), with 44 percent caused by dilated cardiomyopathy. Average age at HTx is  $51 \pm 11$  years, 80 percent are male and average BMI is  $24 \pm 3.7$  kg/m<sup>2</sup>. Since 1998, bi-caval anastomosis has been the standard surgical procedure.

55 percent of the recipients, including our first HTx patient, are still alive. Overall one year survival rate is 88 percent, which has increased to 90 percent after year 2000, five year survival is 78 percent and 50 percent survival is  $12.3 \pm 5.4$  years. The results compare favorably to the ISHLT registry survival.

Rikshospitalet has been a “non induction” centre, using a CNI based, triple drug immunosuppression regimen since 1985. Cyclosporin has traditionally been administered orally preoperatively. Statins were introduced per protocol in 1998, and in 2002 azathioprine was replaced by MMF. Steroids are weaned only in patients with side effects (15 percent) and 98 percent of the recipients are on steroids at one year post HTx. With increasing concern and knowledge about renal failure, induction therapy has recently been introduced for patients facing a high risk of postoperative renal failure and dialysis. More than 60 recipients have been, or are on everolimus in combination with CNI while 50 are or have been on everolimus (without CNI) in addition to steroids and MMF/azathioprine.

Rikshospitalet, together with Swedish and Danish HTx centers has participated in the NOCTET trial that showed an increased GFR for recipients more than one year after HTx introduction of low dose everolimus and CNI compared to standard CNI alone (24 months follow up). In a local protocol, CNIs were replaced by everolimus among recipients with progressive renal failure within first year after HTx with normalization of GFR. Inspired by these results, we initiated the SCHEDULE study, together with Swedish and Danish HTx centers, in de novo heart transplant recipients. In the study arm, patients are started on everolimus in combination with CNI, and CNI is withdrawn between week 7 and 11 post

HTx. In the control arm, CNI is administered traditionally. Primary end point is GFR at one year.

Besides renal failure our scientific focus has been the impact of CAV, CMV and toxoplasmosis infection, hemodynamics, modifiable risk factors, immunological markers and psychological functioning after HTx as predictors for survival.

The LTx program started in 1990. Until October 1, 2010, 323 LTx had been performed in 315 patients older than 18 years of age, including single (89), bilateral (212) and heart-lung (22) transplantations. During the first 10 years, single lung transplantation (SLTx) was the main procedure, accounting for 70 percent of transplants, while in the last 10 years bilateral transplantation (BLTx) has been preferred and is now accounting for 85 percent of the procedures. HLTx has been performed regularly 0-3 times per year in the entire period. The number of LTx per year has gradually increased from 10-15 to 20-30. Average for the last five years is 25.4 LTx/ year, indicating 5.3 million LTx inhabitants.

The ISHLT guidelines (JHLT 2006) are applied in the selection of candidates for lung transplantation, but we have used age over 60 and not 65 years as a relative contraindication. Even with this restriction, the average number of candidates on the waiting list has been approximately 45 in the last five years. This large discrepancy between the patients on the waiting list and the number of transplants indicates a significant number of deaths while waiting for a transplant. In the actual period, 38 patients have died on the waiting list compared to 127 patients transplanted.

The main reason for the extensive waiting list is a large number of referrals of patients with end-stage chronic obstructive pulmonary disease (COPD). The result is a particularly high percentage of COPD-patients, approximately 60 percent of the waiting list and of all the LTx. The gender distribution of COPD-patients without alpha-1-antitrypsin deficiency has changed during these 20 years, during the last ten years women accounted for 56 percent of the LTx because of COPD.

SLTx has been performed via a thoracotomy with partial extracorporeal circulation with cannulation from the groin. BLTx has been performed via a sternotomy on heart-lung machine with or without arresting the heart. We have not performed lobar LTx nor LTx in children under the age of 16 years.



Our results have improved over time, one-year survival in the last ten years is 85 to 90 percent, five year survival is approximately 70 percent.

In spite of the long distances in Norway, we have chosen to have close, life-long follow-up of the patients at the transplant center in order to secure knowledge and experience in all aspects of LTx. We have usually given the LTx patients a triple regimen with cyclosporine, prednisolone, azathioprine or MMF. The management of the immunosuppression is primarily taken care of through phone calls between the patients and our transplantation nurses. All patients are seen at least once a year, and all serious complications with the transplant, like development of BOS, are managed at our hospital. The main problems are, like in most programs, lack of donors and development of BOS.

Main areas of scientific interest have been mechanisms

for the development of BOS and nutrition in the peritransplant period. The aims for the near future are the focus on the donor availability investigating pre-procurement physiology and a program for reconditioning of lungs.

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## Pulmonary Hypertension Council Report

Debbie Levine, M.D., Communications Workforce Leader

The Pulmonary Hypertension (PH) Council is ending a busy and successful 2010 and we are excited that 2011 is showing no signs of slowing down. We are making remarkable progress on many fronts under the leadership of Myung Park (Chair) and Robert Frantz (Vice Chair). Drs. Park and Frantz are carrying on the tradition set by Ray Benza (past-Chair) in developing and strengthening our group. The council continues to expand both in our membership numbers as well as in the multitude of ongoing and new projects that we are dedicated to. We have new workforce leaders who bring with them fresh and original ideas complimented by those who have experience serving in the council.

Our workforces are extremely active with increasing numbers of participants working on a number of ongoing projects as well as initiating new projects with fresh new ideas.

The Registries and Database workforce led by Mardi Gomberg-Maitland and Fernando Torres are building on all of the previous work done by Adaani Frost (past chair of this workforce). They are in the process of creating a grant submission for funding for the database analyses. They are focusing on several topics to evaluate in the database, including:

1. Evaluating if there is a point at which the right ventricle becomes too dysfunctional and may affect outcomes post transplantation.
2. They will also be comparing PH patients post transplantation to understand differences in those with good survival compared to those with poor outcomes.
3. Looking to start developing criteria to determine when a heart-lung should be done, rather than a lung transplant.

Deborah Levine will continue as the Communications Workforce leader. This group continues to update both our workforce as a group as well as serve as a point of communication within the ISHLT society.

The Development Workforce Leader Srinivas Murali continues to develop relationships within all of the pulmonary hypertension areas.

We are looking forward to the ISHLT's 31st anniversary annual meeting set for April 2011 in San Diego. The PH Education workforce (headed up by Dana McGlothlin) council chair and co-chair along with the Programs Committee have worked diligently to increase the number of sessions related to PH in this meeting. There are a record number of original scientific investigations



focused on PH including both basic science and clinical abstracts submitted for the meeting. These topics will be highlighted in oral, mini oral and poster presentation

The scientific program itself is filled with several critical symposiums and sessions related to PH. These sessions set the tone for an outstanding -educational forum as well as a place for some challenging debate and discussions. Topics for the sessions are listed below:

- Challenges in Lung Transplantation for Pulmonary Arterial Hypertension
- Clinical Challenges in Chronic Thromboembolic Pulmonary Hypertention (CTEPH)
- The Latest Concepts and Innovations in PAH
- The Failing Right Ventricle: Mechanisms and

Management

- Pulmonary Hypertension Complicating Left Ventricular Failure: Problems and Progress
- Clinical Controversies in Pulmonary Hypertension: To Treat or Not to Treat? That is the Question

The meeting in San Diego will serve as an opportunity for new and ongoing members of the PH Council to get involved. The ISHLT offers undoubtedly the best opportunity for all of us as pulmonologists, cardiologists and surgeons to come together and encourage each other with new ideas and projects.

We look forward to seeing you in San Diego in April!

## **Nursing, Health Science & Allied Health (NNSAH) Council Report**

**Bernice Coleman, Council Chair and Bronwyn Levvey, Communication Workforce Leader**

The NNSAH Council Workforces have worked hard to achieve some of the goals that were proposed for 2010-2011 including:

**Provide quality clinical and scientific education programs/ symposia for ISHLT 2011/12:** At the 2011 program planning meeting in July, the NNSAH council had two program representatives who successfully submitted and obtained an increase in the number of NNSAH specific symposia. With the abstract deadline recently closed, our council reports a significant increase in the number of research and clinical abstracts submitted to nursing, social sciences, health economics & QoL for the 2011 scientific meeting. In recognition of those who require continuing education units (CEU's), the council reports that CEPTC credits for attending the scientific meeting have been granted by the American Board of Transplant Coordinators for the USA nurses who require them to maintain certification. These credits are also applicable for other international transplant nurses/coordinators (eg Category I credits for Australian nurses).

**Establishing research mentor/mentee relationships:** The research and grants council endeavoured to match research mentors to mentees, and to date communication

between most of the pairs has occurred with some positive feedback. It is hoped that further communication will occur prior to the scientific meeting to facilitate personal meetings.

**Standards & Guidelines Workforce:** Members of the NNSAH council participated in each of the five sections of the Standards & Guidelines currently being produced by the MCS council, and aimed for publication in spring 2011.

**Improved communication to council members:** Letters were emailed to NNSAH constituency, and all ISHLT members who could be potential members, aimed at recruiting new members and volunteers for the various taskforces. We had a great response from potential members seeking to volunteer on our council. Opportunities to improve our communications with our membership also became apparent. We encourage all to update their contact details via the online ISHLT members website to ensure that future communications will successfully reach our member correct address. We encourage all who may have an interest to contact any of the council leadership if you desire to volunteer your council.



## Pathology Council Report

Annalisa Angelini, M.D., Chair

### 1. Antibody-mediated rejection:

Since the Chicago Meeting in April 2010, there have been a number of Skype® conference calls between the Pathology Council Chair and the Co-chairs of the Pathology Breakout Session, held during the “Consensus conference on antibody-mediated rejection (AMR) in heart transplantation” immediately before the main meeting. In consultation with the other pathology attendees the outcome of the session includes our formal report, details of further work to be done and a summary of our discussions for Dr. Kobashigawa’s final report of the conference which will be published soon in JHLT.

Three projects on refining pathological diagnosis of AMR have been identified. We plan to undertake them between now and the San Diego meeting in April 2011, when they will be reviewed by the pathologists involved in the 2010 conference. The first two projects involve the use of web-based digitized biopsy slides to standardize and validate reproducibility of early histopathological features of AMR and of a scoring system for evaluating intensity and distribution of capillary C4d deposition in routinely-processed endomyocardial biopsies. As our third project we will seek to establish a central ISHLT-supported database for collection of anonymized data on cases of AMR linked to web-based digitized slides of their biopsies. This will enable us to clarify areas of uncertainty and thus improve diagnosis of AMR amongst pathologists through education and reproducibility studies. Finally we will seek to publish an illustrated update to the ISHLT 2005 working formulation for biopsy diagnosis of cardiac AMR.

### 2. From the Educational Council (Renè Rodriguez)

There were several conference calls throughout the year. The ISHLT academy was discussed, and considered a very important element of the society by all the councils. Different aspects of the monographs, including demand for them, outreach of these to different councils and costs were addressed. The last volume (No. 4 is now available History of International Heart and Lung Transplantation, edited by James K. Kirklin, MD, Mandeep Mehra, MD, and Lori J. West, MD, PhD). Proposals for satellite meetings to educate HF/Tx Fellows (Pros- and cons- , logistics, demand for, faculty, funding and curriculum for these were considered). During the conference calls there were discussions about several proposals for Symposia that included: infectious disease issues, transplantation in pediatric and adolescent heart failure and transplant care, new horizons in pediatric transplantation, outcomes disparities, AMR in lung, and symposia on AMR in heart. In addition, two papers had final drafts reviewed: “Definitions of Infections in Heart and Lung Transplantation” and “Definition of Infections in Patients Using Ventricular Assist Devices”.

### 3. No reports from other workforce leaders.

Finally, please contact me with your ideas, questions and suggestions at [annalisa.angelini@unipd.it](mailto:annalisa.angelini@unipd.it). All suggestions are welcome.



## **Pulmonary Transplant Council Report**

Lianne Singer, M.D., FRCPC, Council Chair

The Pulmonary Transplant Council continues to focus on an exciting variety of ongoing and new projects under the leadership of Lianne Singer (Chair), David Weill (Vice Chair) and Michael Mulligan (Secretary).

We have two novel registry-based projects under development. Our Registries and Database Workgroup led by Shaf Keshavjee is actively working on a DCD registry with UNOS that will link to the ISHLT registry. The Quality of Life Workgroup, led by Roger Yusen and Lianne Singer, is working on the QUILT (Quality of Life in Lung Transplantation) registry pilot study, which will link patient health-related quality of life measurements with ISHLT registry data.

The Antibody-Mediated Rejection Workforce led by Debbie Levine and Adriana Zeevi will be getting off the ground with a meeting of both the Pathology and Pulmonary Councils at the upcoming annual meeting in San Diego in April.

We actively collaborate with other societies. With the ACCP, we administered a survey of palliative care barriers and practices in lung transplant candidates, which has been submitted as an abstract for ISHLT 2011. With the ATS and the ERS, we are working on an updated review of chronic allograft dysfunction.

The members of the Education Workforce have had a very busy year under the leadership of Chris Wigfield. This group has created the outline and the ground work for the first ISHLT Academy: Core Competencies in Lung Transplantation. This is a very exciting two-day course packed with a comprehensive review of clinical knowledge and essential professional skills required for the surgical and medical care of lung transplant candidates and recipients. The faculty of this course includes

internationally recognized experts in each subspecialty. The ISHLT Academy focused on Heart Transplantation at the last ISHLT meeting was a huge success, and we believe this will no doubt be just as popular and successful.

Our Council is delighted that there are a great number of exciting scientific and clinical abstracts submitted for the upcoming 31<sup>st</sup> annual meeting in San Diego. As is the standard of the ISHLT, this year's meeting promises a stimulating scientific session filled with original investigations from all subspecialties of lung transplantation.

The ISHLT Program for the 31<sup>st</sup> annual meeting in April in San Diego is filled with a significant number of sessions and symposia focused on multiple facets of lung transplantation. A full description of each of these sessions can be found in the preliminary program on the ISHLT website. We will highlight these in more detail in the next LINKS issue closer to the meeting. Some of the highlights and topics of these sessions include: Preserving microvascular function in lung transplantation, optimizing lung allocation, AMR in lung transplantation, challenges of lung transplantation for PAH, ECMO in lung transplantation, donor organ optimization including ex-vivo perfusion, obliterative bronchiolitis, experimental models of lung transplantation and many more.

We are expecting a very exciting year at the annual meeting in April and hope to see everyone there participating in all of these sessions!

Happy New Year to all!