

CST News



Welcome to CST News. This newsletter is sent to all CST members and is posted on the CST Website. CST News is published three times a year by the Canadian Society of Transplantation. Views expressed in news and feature articles are those of the individuals quoted.

CST Communication Committee: John Gill and Patrick Luke

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President – Dr. Lori West President Elect – Dr. James Shapiro Past President – Dr. Ken West Treasurer – Dr. Greg Knoll
Members at large – Dr. Lee Anne Tibbles, Dr. Marcelo Cantarovich, Dr. Tom Blydt-Hansen, Ms. Susan Chernenko

PRESIDENT'S MESSAGE

Dear CST members,

In its 25th year, our Society continues to grow and expand its activities under the mandate to serve as *the voice of transplantation in Canada*. We can anticipate exciting times in the year ahead, as a number of national issues come forward for discussion, and as we continue to explore important links internationally. Society members are serving in leadership positions in an increasing number of transplant-related professional associations, as well as in research and policy forums, bringing an important voice both to the national and international transplant communities. Through these and other efforts of the Society, we will strive ultimately to improve outcomes of transplant patients.

Committees: The various committees within CST are becoming increasingly active and well-organized, and will contribute further to the robust nature of our dialogue as a community. The special interest groups, comprised of five organ-specific working groups, the Pediatric group and the HLA group, are bringing issues forward in each of their particular domains, thus encouraging in-depth consideration by the Society. Of the ad-hoc committees, the Policy Committee, in particular, chaired by Ken West, will have a renewed mandate for consideration of complex matters impacting on the interchanges amongst CST and industry, government and other interested parties in transplantation medicine and science, including Health Canada, Canadian Standards Association and Canadian Council for Donation and Transplantation. The Communications Committee chaired by John Gill will be continuing the critical dissemination of information to our growing membership through the newsletter and website, in order to preserve the unique sense of identity and community of the Canadian transplant community.

Membership: Our total membership now exceeds 450 individuals, with the most rapid growth in the past two years being in the category of 'associate member', which includes trainees and allied health professionals. We welcome the active input of all members across the broad range of individuals with a professional interest in transplantation in clinical practice, research and education. This year, we

particularly hope to encourage further involvement in the CST by members of the transplant community in Quebec, which has historically been under-represented in our membership. We invite all members to join in this 'membership drive' at the local level by high-lighting Society activities.

Trainees: The Society will maintain its particular effort on enhancing interest in transplantation for trainees through emphasizing education and career opportunities. The "Trainees' Day" will continue to be held at the annual meeting, and reflects the growing involvement in transplantation of trainees at different levels and with diverse academic backgrounds. This forum will continue to be showcased amongst all members as a high-caliber educational and networking opportunity. The Society will also maintain its role as a partner in educational initiatives, including Kidney Foundation/Canadian Society for Nephrology/CST fellowships and the CIHR Young Investigator forum, and will seek new partnerships to broaden and deepen these crucial activities.

Meetings: Our 2006 annual scientific meeting in Mont-Tremblant was a distinct success under the direction of Greg Knoll with, as always, unwavering assistance from H el ene Samson and her administrative team. Lee Ann Tibbles is heading the program committee for the 2007 meeting in Banff, with plans for a special celebration to mark the 25th anniversary of the CST. Society members are also instrumental in the organization of the upcoming Basic Science Symposium of The Transplantation Society, to be held in Halifax in Sept. 2007, under the leadership of Ken West.

In closing, the CST Executive Committee genuinely wishes to serve the interests of its members, and will welcome comments and suggestions from all members with enthusiasm.

Lori West, MD, DPhil, FRCPC

Mission Statement – Canadian Society of Transplantation

1 It is the purpose of the Canadian Society of Transplantation to further all aspects of transplantation in Canada.

2 To provide and maintain a national professional forum for physicians and surgeons, scientists and others occupied in clinical and scientific aspects of transplantation.

3 To promote the educational and scientific advancement of the broad discipline of transplantation.

4 To study and to comment appropriately upon the impact of educational and scientific advances and of changing social and economic developments as they relate to the maintenance of high standards of patient care among its members.

5 To collaborate with other national and/or regional organizations having responsibilities or mutual interests related to the attainment of the Society's objectives.

CANADIAN SOCIETY OF TRANSPLANTATION

Highlights of the CST Annual Scientific Meeting – Mont Tremblant, Québec, March 2-5, 2006

CLINICAL ABSTRACTS SESSION

The 2006 Annual Scientific Meeting in Mont Tremblant highlighted some exciting clinical research being conducted in Canada. In the oral presentation session, Dr. Bhanu Prasad from Vancouver presented his work on the utility of flow crossmatch in living kidney transplantation. Unlike the experience in deceased donor transplantation, he found that patients with a positive or negative flow crossmatch had similar rates of acute rejection and graft survival. This novel finding could have a major impact on the approach to crossmatching in the living donor situation. Dr David Rush from Manitoba provided an update on his Canadian multi-centre trial examining the role of protocol biopsy in renal transplantation. In his presentation, Dr Rush showed that the incidence of subclinical rejection was very low at all biopsy time-points and there were no significant differences between the protocol biopsy group and the control arm with respect to chronic pathologic changes, renal function or graft survival. This important Canadian study will likely alter the role of protocol biopsies in transplant practice. In the area of heart transplantation, Dr Marcelo Cantarovich from Montreal presented data on his novel approach to renal dysfunction following heart transplantation. He showed that stopping a calcineurin inhibitor (“retirement”) under prolonged coverage of either basiliximab or daclizumab resulted in a substantial improvement in creatinine clearance without increasing the risk of acute rejection. This important new strategy will likely be replicated at other centres and we await these exciting results.

In the poster sessions there were 80 clinical abstracts presented highlighting some excellent Canadian researchers. Dr Jennifer Vethamuthu and colleagues from Ottawa evaluated ganciclovir levels in a group of pediatric transplant recipients. They found subtherapeutic levels in 42% of cases. Inadequate levels occurred with both oral as well as intravenous therapy. The authors concluded that therapeutic drug monitoring might be warranted given this high degree of variability. In another

featured poster, Dr Lakey from Edmonton examined the role of machine perfusion of donor pancreas prior to islet isolation. For entry into this study, they used a clinical scoring system to select only suboptimal donor pancreas. These suboptimal organs were placed on a standard kidney perfusion machine and perfused an average of 5 hours. The suboptimal organs that underwent machine perfusion had higher islet yields than a control group of pancreas that did not undergo machine perfusion. This preliminary report suggests that the yield from suboptimal pancreas donors may be improved with machine perfusion. The authors plan to study machine perfusion from the time of procurement to see if further gains in islet yield can be achieved. Dr Sarah Armstrong and her colleagues from London, Ontario presented data on clinical correlates of cardiac allograft vasculopathy. They found that patients with severe coronary angiographic abnormalities often had normal ventricular function and elevated filling pressures at rest but with physical stress were unable to increase output. The authors concluded that these findings should be taken as a sign of significant cardiac vasculopathy in the heart transplant recipient.

-Greg Knoll

WINNERS- 2006-CST CLINICAL TRAINEE ABSTRACTS

Elizabeth Haddad, Chatham ON
Marylise Boutros, Kirkland QC
Bhanu Prasad, Vancouver BC

BASIC SCIENCE ABSTRACTS SESSION

At the CST meeting this year, 35 basic science abstracts were presented. The vast majority of the abstracts were of very high quality. Due to space constraints, only podium and highlighted poster abstracts are summarized here.

Allograft viability and survival may be reduced due to ischemia-reperfusion injury. This was by far the most heavily discussed topic at this year’s meeting. There were a host of abstracts that addressed the prevention of organ damage from ischemia-reperfusion injury using novel techniques such as shRNA and siRNA silencing. Researchers from the University of Western Ontario showed that it was feasible to reduce murine renal injury with RNA silencing of Fas (Du), caspase 3 (Zhang), caspase 8 (Du and Zhang), complement (Zheng) and IDO (Mohib).

In addition to RNA silencing, other different mechanisms to prevent chronic graft injury were investigated. Specifically, for lungs, Sato showed that MMP inhibition had a role in preventing bronchiolitis obliterans with dose-dependent differential effects on apoptosis and collagen accumulation. Nguan and colleagues showed that IL-2R blockade may prevent renal damage via reduction of apoptosis after ischemia reperfusion injury. As well, Laplante et al. showed that extracellular matrix fragments from apoptotic endothelial cells leads to survival of fibroblasts, indicating that this mechanism may be targeted in the prevention of chronic allograft damage.

In any type of vascularized organ graft, vascular factors may affect transplant survival. Therefore, the deleterious effect of cyclosporine on endothelin-1 and nitric oxide and vascular injury vs. sirolimus was discussed by Ramzy and colleagues. Their findings support the basis and rationale for calcineurin inhibitor (CNI)-avoidance and CNI-withdrawal. Furthermore, Barama showed that sirolimus combined with an ACE inhibitor prior to occurrence of glomerular damage may prevent podocyte damage and FSGS in a 5/6 nephrectomy model, despite reports of sirolimus promoting proteinuria.

With respect to tolerance and immunosuppression, there was a general reassessment of the role of tolerance in transplantation. A more focused look at tolerance mechanisms in the early part of life was presented. Fan et al. created a model of ABO incompatible heart transplantation using gene therapy to study neonatal B cell tolerance in ABO incompatible heart

transplants. In a more mechanistic study, Hofmann from the same group investigated the critical role of the regulatory CD4+CD25+Foxp3+ T cell in neonatally tolerized organ recipients. In a preclinical model, CD45RB mAb, which induces tolerance in mice, was shown to prolong survival in a non-human primate transplant model. Importantly, Luke and colleagues showed that it also acted synergistically with tacrolimus, indicating that CD45RB mAb may become a clinically useful induction agent. Vu from Boston investigated the favorable role of costimulatory molecule OX40L blockade in combination with anti-CD40L mAb therapy in memory T cell-associated rejection in a murine skin transplant model. Ultimately, inhibition of these memory T cells may enable long-term engraftment in primate transplant models that have previously failed CD40L mAb and CTLA4lg monotherapy.

Although there appears to be limited utility in donor specific bone marrow transfusion in clinical transplantation, vascularized bone transplantation with stable macrochimerism appears to be able to induce tolerance in murine transplant models. In fact, Hao et al. showed that this radically novel approach in combination with standard immunotherapy prevents allo- and xenograft rejection.

Several presentations assessed the ability to predict transplant outcomes. Anraku et al. retrospectively compared gene expression profiles from lung transplant donors and noted that 3 gene ratios predicted outcomes with high accuracy. This finding needs to be prospectively reassessed in donor lung selection. Acott and colleagues assessed the in vitro response of BK virus to a host of immunosuppressive drugs and found that cyclosporine and MMF (and not FK506) appeared to have favorable inhibitory activity, which may in part explain the emergence of BKVAN during the FK506 era. As well, it may indicate that patients on FK506/MMF with BKVAN should be weaned off FK506 in favor of reduction of MMF.

-Patrick Luke

WINNERS - 2006- CST BASIC SCIENCE TRAINEE ABSTRACTS

Xiufen Zheng, London ON
Xiaohu Fan, Toronto ON
Masaaki Sato, Toronto ON

Please visit us:
www.cst-transplant.ca

2006 CST LIFETIME ACHIEVEMENT AWARD DR. CARL CARDELLA



Dr. Cardella was awarded the 2006 CST Lifetime Achievement Award at the CST Gala in Mont-Tremblant last March.

After completing his clinical training in General Internal Medicine and Nephrology at the University of Toronto, Dr. Cardella began his research training in cell biology and immunology at a medical research laboratory in London, England in 1972. In 1974, Dr. Cardella began his staff career as a nephrologist with a special interest in renal transplantation at the Toronto Western Hospital. At that

time, he established a research program directed towards understanding the mechanisms of immune responsiveness and directed a laboratory that produced and immunosuppressive drug, rabbit antithymocyte serum. In 1985, in conjunction with Dr. Tirone David, Dr. Cardella helped to re-establish the Heart Transplant Program at the Toronto Western Hospital. In 1990, after the merger with the Toronto General Hospital, the renal and heart transplant programs were transferred to the Multiorgan Unit at the Toronto General Hospital. In 1987, he assumed the responsibility of Director of the Division of

Nephrology at the Toronto Western Hospital and after the merger with Toronto General Hospital in 1990, he continued in his role as Division Director until March 2001.

Dr. Cardella has over 100 refereed publications relating to transplantation and has participated in several national and international programs to increase organ donation and to promote transplantation. At the present time, Dr. Cardella's research interest is in basic immunology and clinical transplantation. His administrative roles include Director of Medical Services for the Toronto General Hospital, Chairman of the Medical Advisory Committee (2000-2005), University Health Network and Medical Program Director for Advanced Medicine and Surgery, University Health Network.

Dr. Cardella concluded his address at the Gala Dinner with these words: *'Transplantation is a challenging and rewarding clinical success story. Over the last 30 years, I have learned many valued lessons from my current and former colleagues, from my mentors, from trainees and students and from my patients. The transplant specialist today is faced with the same dilemma as we had many years ago – to find a balance point. The challenge to improve patient outcomes, succeed academically and to gain new information has to balance with the needs of family, friends and personal development. Tonight is so very special to me because my two worlds – transplantation and family and friends – have come together to make this a night I will never forget. I want to thank the Canadian Society of Transplantation for this honor which I will treasure for ever.'*

Report from the organizing committee for the 2007 CST Annual Scientific Meeting

Planning for the 2007 Annual Meeting at the Banff Springs Hotel in Banff Alberta is well underway. The themes for the 3 Plenary Sessions have been chosen. Theme One will be Ischemia/Reperfusion Injury, including the clinical topic of extended criteria donors, and some basic science insights. Theme Two is Management of the Sensitized Patient, and the Third Theme is Transplant Co-Morbidities. We are looking for suggestions for a debate topic, and welcome suggestions from the membership regarding excellent speakers that they would like to see invited. For those non-skier members, we have arranged a reserved block of appointments at the Willow Stream Spa which can be booked prior to the meeting. Further updates will be available with the next newsletter. Please plan to attend the 2007 Annual Scientific Meeting in Banff, March 15-18!

-Lee Anne Tibbles

ANNOUNCEMENTS

2005 Recipient of the Medal for Research Excellence: Dr. Anthony Jevnikar

The prestigious medal is awarded each year by the Kidney Foundation of Canada to honour a Canadian researcher whose work is recognized by his peers to have significantly advanced the treatment of kidney disease and related conditions.

Congratulations to Dr. Jevnikar!

Meeting in Boston organized by the CST Kidney Group (Ed Cole, Chair)

Greg Knoll and John Gill invite all interested investigators to attend the first meeting of the Canadian Kidney Transplant Clinical Group, to be held during the WTC in Boston, as follows:

Date: Tuesday, July 25, 2006

Time: 0830-1030

Hotel: Fairmont Copley in Copley Square, 138 St. James Avenue, Boston (1 block from the Convention Centre)

Room: The Back Bay Room

Top 40 under 40 – Patrick Luke, surgeon

The honorees for this annual event are drawn from an initial list of 1,200-1,400 nominations from across Canada. From this year's shortlist of 100, a panel of 29 business and community leaders selected the top 40 based on five criteria: vision and leadership; innovation and achievement; impact; growth/development strategy; and community involvement. Congratulations Dr. Luke!

Upcoming AST Board Elections

Two Canadians are nominated: Drs Lori West and Tony Jevnikar. Please be sure to vote to ensure Canadian presence on the AST Board.

CST MEMBER PROFILE



Christopher Nguan, raised in Halifax NS, finished his MSc in molecular biology at the University of Western Ontario. He returned home to obtain his medical training at Dalhousie University and subsequently completed a urology residency at the University of British Columbia and has nearly completed a punishing 2 year ASTS-certified surgical fellowship training program at the University of Western Ontario.

A gifted surgeon, Dr. Nguan hopes to augment the formidable living donor transplant volumes at the University of

British Columbia, where he will be an Assistant Professor of Surgery. His research at the University of Western Ontario has put him in perfect position

to optimize the function of the deceased donor transplants as well. At the American Urologic Association meeting in May 2006, Dr. Nguan delivered a podium session addressing the advantages of dual en bloc adult kidneys for extended criteria donors. At the World Transplant Congress in July, he will deliver another podium presentation discussing the use of perfusate-based verapamil to protect allograft function. His bench research also investigates the use of carbon monoxide and IL-2R blockade in the protection of the allograft during ischemia-reperfusion injury. As a testament to his work ethic, he has a total of 7 accepted abstracts at the upcoming WTC Meeting in Boston and presented 9 papers at the CST meeting in Tremblant this past year.

Although his colleagues and mentors at the University of Western Ontario would have liked to keep him in London, his wife, Angela, has drawn him back to the University of British Columbia. The CST members look forward to a great amount of productivity and innovation with Dr. Nguan's new found independence in Vancouver.

CST ASSOCIATE MEMBER PROFILE



Janice Bissonnette is an Advanced Practice RN and Manager for the Renal Transplant Program at The Ottawa Hospital. Born and raised in Trenton, Ontario, Janice obtained a BScN at The University of Ottawa in 1985. The majority of Janice's clinical practice occurred with in the Critical Care areas at The Ottawa Hospital, with teaching and academic roles at both the college and university levels. Janice completed her Masters in Nursing Science in 2000 from The University of Ottawa, followed by a Post Masters Acute Care Nurse Practitioner Degree from the University of Toronto

in 2001. Most recently Janice received a Graduate Admissions Scholarship for PhD studies in Nursing Science and is entering her second year of study. The focus of her doctoral work is the development and evaluation

of interventions tailored to medication adherence issues for the Adult Renal transplant population. A large part of this work looks at the influence Health care providers have on adherence decisions.

Janice became a member of the Renal Transplant Program at the Ottawa Hospital in 2005. As the first Advanced Practice Nurse for the program, Janice has been instrumental in establishing an Inpatient post-transplant clinical pathway, standardized regional transplant referral process and a Nurse Practitioner led Post-Transplant Chronic Kidney Disease Clinic. Working in collaboration with the renal transplant team, Janice has presented their work at the CST 2006 meeting in Tremblant and CANNT in 2005.

Outside the clinical setting, Janice maintains a joint appointment with the University of Ottawa School of Nursing and is working with RNAO to develop Nursing guidelines in support of decision making for patients with ESRD. It does not end here. Janice has an active family life, husband Robert and three teenage daughters keep her on track. Janice is a mother, wife, skier, reader and life long learner. The CST welcomes Janice to the Society.

BASIC SCIENCE SYMPOSIUM OF THE TRANSPLANTATION SOCIETY

*Translating Knowledge to the Clinic
Halifax, Nova Scotia, 5-8 September 2007*

Topics to be covered at the BSS-2007 meeting in Halifax:
Innate-Adaptative Immunity; Allograft Injury; Tolerance and Tregs; Immunological Niches;
Imaging of the Immune System; Gas Biology; Gene Regulation in the immune System.

The meeting will take place at the Westin Nova Scotian, 1181 Hollis Street, Halifax.

For more information, please visit the BSS Website at <http://www.bss2007.ca> where more information will be posted as it becomes available.

