

Rapport



Pushing The Frontiers

LONDON'S LEGACY IN TRANSPLANT RESEARCH LIVES ON



PLUS...

ALUMNI MAKING A DIFFERENCE

A DAY IN THE ER

YEAR ONE IN WINDSOR



Pioneering Miracles

BY KRIS DUNDAS

Photos by Shawn Simpson

For over three decades transplantation has been one of London's pinnacle examples of a world-class translational research program that integrates the work of basic scientists and clinicians in a common goal: **saving lives.**

Dr. Bill Wall (MD'70) vividly remembers the snowy day in 1978 he went to Toronto airport to collect the first vial of cyclosporine to arrive in Canada. It was the “magical white powder” transplant surgeons had been waiting for – a drug that could prevent the immune system from attacking a transplanted organ. Since then the London transplant program has never looked back.



TRANSPLANTATION RESEARCH IN LONDON RUNS THE GAMUT FROM BASIC MOLECULAR SCIENCE TO EXPERIMENTAL MICROSURGERY TECHNIQUES TO APPLICATION IN CLINICAL TRIALS. THE PROGRAM IS WORLD-RENOWNED FOR ITS TRANSLATIONAL NATURE, TURNING DISCOVERIES FROM THE LAB INTO REAL SOLUTIONS FOR PATIENTS (Photo courtesy of Transplant Program).

The enormous research enterprise crossing multiple departments at Schulich, Lawson Health Research Institute and Robarts Research Institute has been the engine driving the clinical success, and continues to push the boundaries of transplantation. The Multi-Organ Transplant Program at London Health Sciences Centre (LHSC) has achieved dozens of firsts, including leading the first clinical trial in Canada on cyclosporine, the first liver transplant in Ontario, the first heart-lung transplant in Canada, the world's first liver-bowel transplant, and the first living donor liver transplants in Canada. With two new Co-Directors in place, Dr. Patrick Luke and Dr. Anthony Jevnikar (BSc'76, MSc'77, MD'81), and an arsenal of top scientists and clinicians, the program is poised to build a brilliant future, inspired by the legacy of the past.

The Legacy

It all started in 1972 when University Hospital opened and it was determined transplantation would be a focus. At that time the results were dismal. Most died within months and few thought there was a future in transplantation. “We had people here of vision,” says Wall. “We had individuals like Calvin Stiller who knew someday organ transplantation would be widely applicable and have a high success rate.”

Dr. Stiller led the development of the transplant program in London and was Director until 1997. He also led the groundbreaking Canadian study on cyclosporine in kidney recipients. Cyclosporine proved to be a “quantum leap” in organ transplantation, pushing the success rate of kidney transplants to 80 per cent, and sparking a renewed interest in other transplants such as liver and heart.

“We got the drug before anyone else in Canada because of our connections with the group in Cambridge, England who were the first ones to prove its use both in the laboratory and the clinic,” explains Wall, who trained as a transplant surgeon in Cambridge in 1975 and 1976. “It was exciting to go from a miserable level of failure to a high level of success within several years. It was a wonderful experience to see these patients who were facing certain death from organ failure have their lives saved.”

A pioneer himself, Wall recently stepped down as Director of the Multi-Organ Transplant Program after 12 years at the helm. In January 2009 he was named to the Order of Canada for his contributions to liver transplantation and organ donation awareness.

The Research

Today, dozens of researchers advance transplantation from many angles. From basic molecular studies of the immune system, to microsurgery models of transplantation, to understanding the injuries to organs in the process of removal, storage and transportation, to clinical trials on immunosuppressive drugs – the research covers the full spectrum. “Every member of our current group and every new member as we

FOR MORE ON THE TRANSPLANT PROGRAM VISIT www.lhsc.on.ca/transplant

TRANSPLANTATION IN CANADA (2008)

- 4,380** Total on transplant waiting list
- 2,083** Total transplants in Canada
- 215** Number who died on waiting list
- 25** London organ donor rate per million people
- 13** Canadian organ donor rate per million people

Source: Canadian Organ Replacement Register, 2008

recruit ... has to want to solve the fundamental problem of transplantation,” says Dr. Jevnikar, a nephrologist and clinician scientist recently named the Canadian Institutes of Health Research Wyeth Chair in Transplantation.

It’s what transplant surgeon Dr. Luke, also a clinician scientist, calls a “bench to bedside and bedside to bench” continuum. “Every patient will benefit from the research that we do.”

One quarter of transplant patients at LHSC are in clinical studies (about 160 organs are transplanted annually here). In total, the transplant program has attracted \$32.9 million in research grants over the past five years and published 229 publications in peer-reviewed journals. It is the only centre outside the United States to receive National Institutes of Health (NIH) funding to study transplant tolerance. The program also has three endowed research chairs.

Dr. Joaquin Madrenas, Robarts Scientist, holds the Canada Research Chair in Transplantation and Immunobiology. His work focuses on T-cells – the ‘generals’ of the immune system’s army that attacks a transplanted organ. His research is essential to improving outcomes and ensuring recipients don’t return for a second or third transplant, which often happens, particularly in kidney transplants.

“What we are trying to do is reach a state in which we know what signals can turn off the immune system. As soon as we have those signals, we can reproduce them with certain types of medication. We still don’t know exactly what these signals are, but we are closer than we were a few years ago,” says Madrenas noting that they use less medication now to achieve transplant survival than 20 years ago.

Another internationally renowned success story in transplant research is microsurgery, an area pioneered by the late Dr. Robert Zhong. “He developed in the microsurgery laboratory here the technique for transplanting all organs and tissues in rodents and it provided an enormous platform for transplantation models in which we could study rejection, the effectiveness of immunosuppressants or the combination of immunosuppressants,” explains Wall.

It was exciting to go from a miserable level of failure to a high level of success within several years. It was a wonderful experience to see these patients who were facing certain death from organ failure have their lives saved.

DR. BILL WALL

“Now we have a shelf of the best options for patients.”

More than 150 microsurgeons have been trained in London. The program has also trained hundreds of basic science graduate students, postdoctoral fellows and clinical fellows.

The Future

With all of the program’s success, they are still unable to help everyone because of a shortage of donated organs. “The results have never been better than they are at the present time in transplantation,” says Wall. “But at the same time, the numbers of patients waiting for transplants has never been greater, the time of waiting has never been longer and the chance of dying while waiting has never been higher.”

Some of the solutions will come from the laboratory. Prevention of chronic disease is key; also designing better medications and finding ways to prevent organ injury. But there is also the promise of stem cells and regenerative medicine – repairing or remaking a failing organ. Madrenas says “Transplantation should be a step to fully regenerative medicine ... but this is a global initiative at very, very early stages.”

Not waiting on this futuristic solution, the team is working hard to improve the success rate and health of transplant recipients, and also expanding organ retrieval. London scientists and clinicians are national leaders in transplanting organs after cardiac death, a relatively new phenomenon. They are also continuing to advance living donor donations, particularly in liver and kidney transplants.

One of the milestones for the program will undoubtedly be the Matthew Mailing Centre for Translational Transplant Studies, a new 10,000 square-foot

facility expected to open at LHSC in 2011. The centre will be close to the Multi-Organ Transplant Unit at University Hospital, which Luke says will be a huge advantage. “Five hundred feet from where patients are taken care of, we’ll be doing studies on medications they will receive in five years. It’s amazing.”

Jevnikar is also hoping the centre will help change some of the complacency he sees about the transplant program. “We have a mature program that has been excellent for so many years, sometimes we take that for granted,” says Jevnikar. “If you have a miracle every day, it can just become routine ... but they’re still miracles.”

Madrenas agrees. “Transplantation is unique (in London) because we have been putting resources into it. If we don’t continue to do that, we lose our competitive edge.”

For its part, Schulich Medicine & Dentistry is helping to support a new transplant scientist and surgeon, Dr. Alp Sener, through the Schulich Clinician Scientist Program, raising funds to establish an endowed research chair in memory of Dr. Zhong and plans to announce a unique translational immunology centre within the year. 🌐



SURGEON DR. PATRICK LUKE (LEFT) AND NEPHROLOGIST DR. ANTHONY JEVIKAR WERE NAMED CO-DIRECTORS OF THE MULTI-ORGAN TRANSPLANT PROGRAM EARLIER THIS YEAR