Research in Manitoba changes lives.

Research Manitoba

—

Karly

Karly had been on peritoneal dialysis for a year when, at 15, she received a transplanted kidney from her mother. Despite missing a lot of school prior to and immediately after the transplant, in the fall of 2016, Karly is off to McGill University in Montreal to study biomedical sciences with the intention to pursue medicine.

"My transplant has given me an education, freedom, and independence so that I am more than just my illness. This research provides people with a new chance at life, an opportunity to succeed, and be happy."

- Karly

IMPACT REPORT // KIDNEY TRANSPLANT RESEARCH

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Dr. Peter Nickerson

Dr. Peter Nickerson is Professor of Medicine and Immunology, and Vice Dean [Research] Rady Faculty of Health Sciences at the University of Manitoba and the Medical Advisor [Organ Transplantation] Canadian Blood Services

"Research may seem like it takes a long time to go from discovery to patient benefits — but it wasn't long ago that we thought transplanting an organ was impossible. Without research, without the skill, knowledge and drugs — we know that many patients would have likely died on dialysis."

- Dr. Nickerson

Research in Manitoba
is a smart investment.

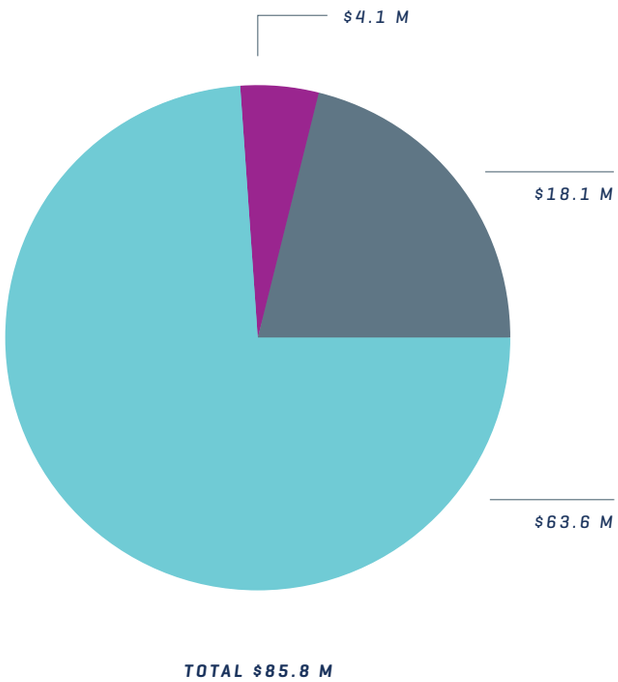
Since 1997

$85.8 million
from ***provincial, national,*** and ***international*** sources has been invested in kidney transplant research and its translation to policy and practice.

$4.1 million
contributed by Manitoba

$18.1 million
additional investments flows in to Manitoba for research

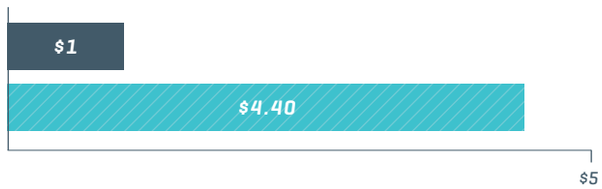
$63.6 million
for translation as well as networks mostly outside of Manitoba



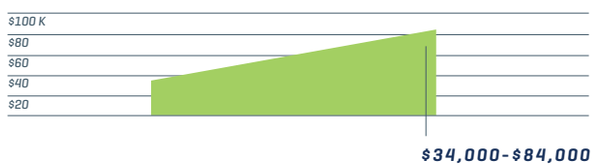
Successful transplants reduce the need for expensive and intrusive dialysis, but more people are diagnosed with kidney disease everyday as diabetes, obesity and other factors increase.

We are mitigating this rate of increase with every successful transplant — reducing the burden of costs to our health system and improving each person's quality of life.

$4.40
net return to the province, for every Manitoba dollar invested in kidney transplant research



$34,000-$84,000
saved for each successful transplant patient per year after the second year post transplant

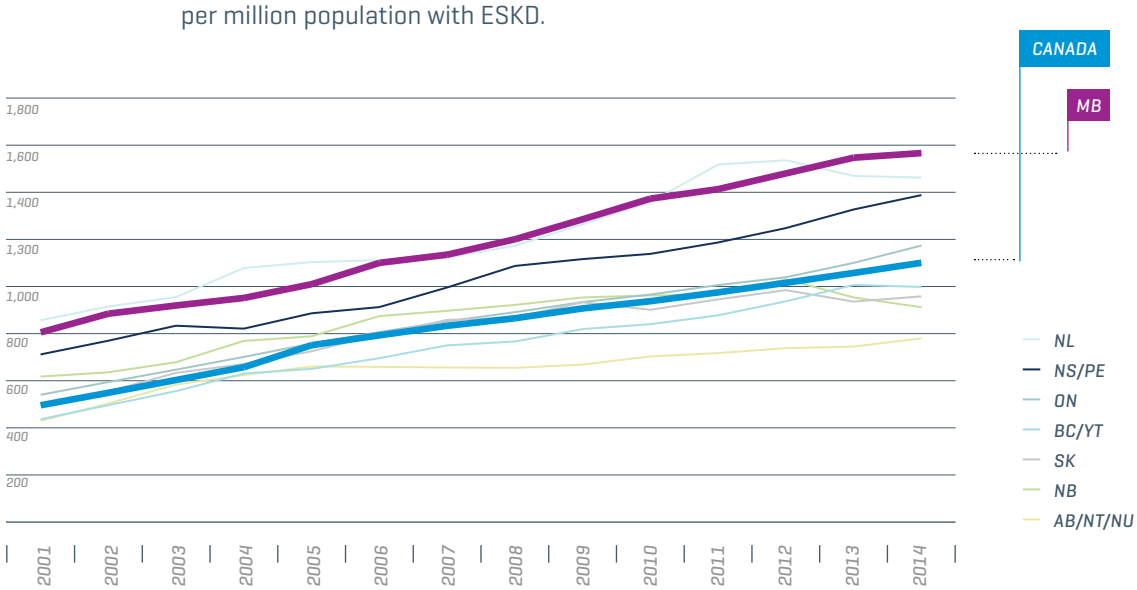


End stage kidney disease

From 2001 - 2014

In the past one and a half decades, the number of people living with ESKD has been increasing in Manitoba and Canada. Among all the provinces, **Manitoba** has the highest number of people per million population with ESKD.

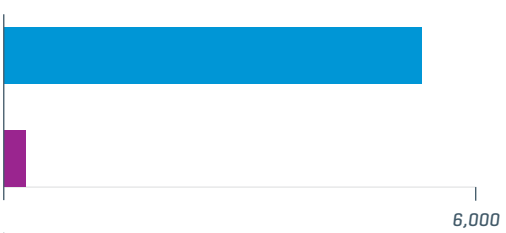
*ESKD is the **#1 cause** of kidney failure.*



In 2014

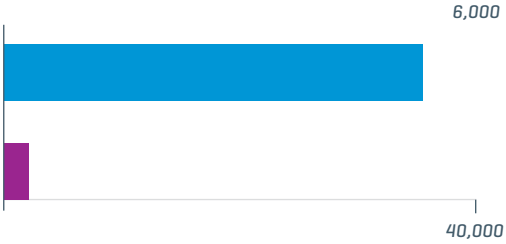
5,269
New cases of ESKD in Canada

275
New cases of ESKD in Manitoba



35,281
Canadians living with ESKD

2,084
Manitobans living with ESKD



IN 2014

***58.6%** of Canadians living with **ESKD** were receiving some form of dialysis*

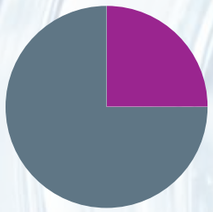
Transplant is better than dialysis.

Dialysis and transplants save lives, but...

Patients with kidney transplants live longer and enjoy a better quality of life.

patients on dialysis spend

up to 6 hours per day,



3-4 days per week,

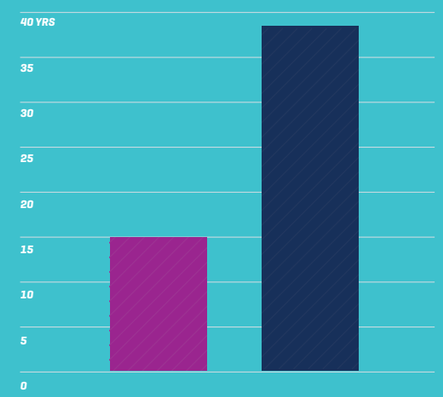
receiving the treatment that keeps them alive.

*The **socio-economic impacts** include improved quality of life, a longer lifespan and improved productivity.*

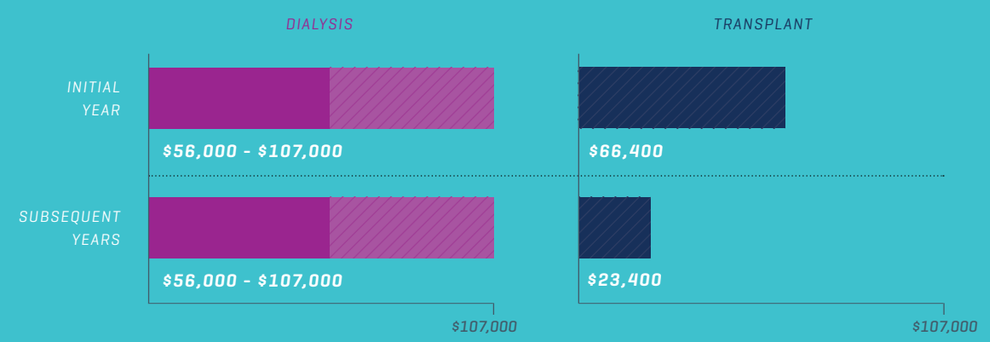
An individual with ESKD between the ages of 20-24 years can survive an additional:

14.9 yrs
on dialysis

38.4 yrs
with a transplant



Treating one person on dialysis costs between $56,000 and $107,000 per year. Health care services for a patient who undergoes a kidney transplant cost approximately $66,400 in the year of the transplant and $23,000 per year thereafter.



Milestones in Manitoba and Canada.

"It's impossible to know how many people we have affected, but through standardization alone, we have most definitely impacted thousands of patients across Canada."

— DR. PETER NICKERSON

The situation before research investment:

BETWEEN 1981 AND 1999, TRANSPLANTED KIDNEYS WERE LOST DUE TO UNDETECTED ANTIBODIES

> Between 1981 and 1999, the number of new patients with end stage kidney disease (ESKD) in Canada increased by 7.3% per year.

> Dialysis was the de facto treatment despite the fact that transplants prolong survival, improve quality of life, and are more affordable.

> To determine kidney graft performance, creatinine levels and clinical symptoms were monitored but, subclinical rejection could have already happened.

> Serologic cross matching was used.

early 1990s

Dr. David Rush pioneers surveillance biopsies. Reports a high prevalence of subclinical rejection, while clinically the kidneys appear normal.

Serologic cross-matching of donors and recipients means 10% of transplants are rejected early due to antibodies. Better matching is required.

1998

Randomized Control Trial proves treatment of subclinical rejection improves outcomes.

2000

A flow cytometer was purchased. Retrospective analysis of tissue samples showed great promise for better donor / recipient matching. Flow cross-matching improves donor/recipient compatibility. One-year post-transplant rejection rates drop from 10% to 2%. Published paper on flow cross-matching in 2001 receives 114 citations.

2003

A paper published in this year was a systematic review of literature and cited 206 times. This was required reading in a 2005 consensus workshop that changed the national standards of care.

2004

Dr. Rush leads multi-centre Canadian Randomized Control Trial which finds that the use of immunosuppressant drugs reduces subclinical kidney rejections. But the required diagnostic biopsies were causing inflammation, leading to scarring associated with premature rejection. Hence, frequent and non-invasive diagnostic tests were needed for the treatment of scarring. Dr. Peter Nickerson and his team undertook this challenge.

2005

Recommendations come forth from two consensus conferences: flow cross-matching pre-transplant should be an integral part of the standards of care across Canada, and the kidney sharing program should be developed.

2006

Canadian diagnostic labs begin standardization of flow cross-matching, led by Winnipeg.

2008

On Dr. Nickerson's team, Dr. Juliet Ho develops urine tests that detect inflammation and scarring early.

2009

Kidney paired donation program pilots are underway in three provinces.

2010

Kidney Paired Donation Program goes national.

2012

Manitoba's De Novo donor specific HLA antibody post kidney transplant study is published. It is now in the top 1% of citations in the academic field of clinical medicine. The National Organ Waitlist is launched.

2013

The Highly Sensitized Donor Program is launched.

2014

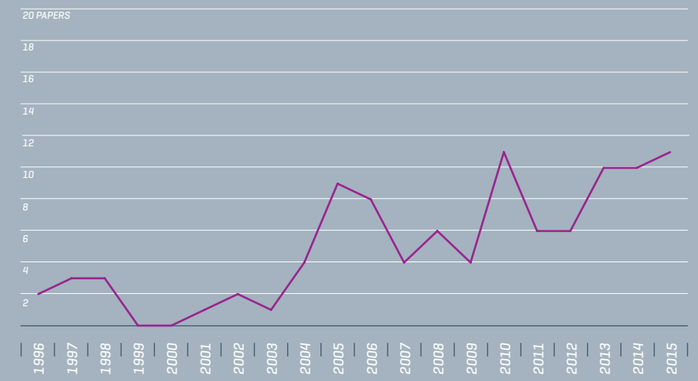
Subclinical assessment pre- and post-transplant allows for faster intervention, reducing kidney rejection.

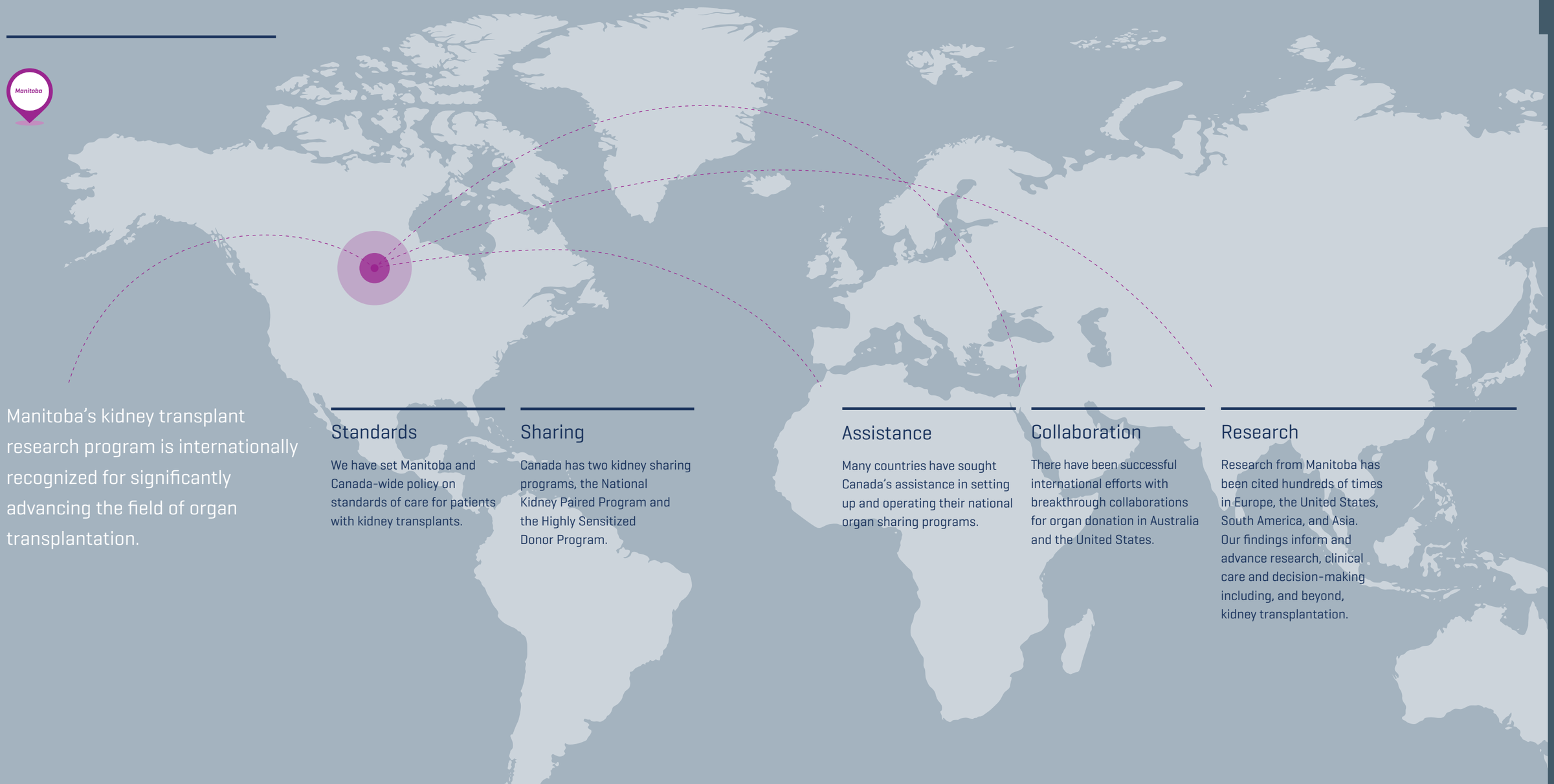
Manitoba's world-class reputation.

The number of papers published is increasing

11
Papers published in **2015**

101
Papers published from **1996 to 2015**





Manitoba's kidney transplant research program is internationally recognized for significantly advancing the field of organ transplantation.

Standards

We have set Manitoba and Canada-wide policy on standards of care for patients with kidney transplants.

Sharing

Canada has two kidney sharing programs, the National Kidney Paired Program and the Highly Sensitized Donor Program.

Assistance

Many countries have sought Canada's assistance in setting up and operating their national organ sharing programs.

Collaboration

There have been successful international efforts with breakthrough collaborations for organ donation in Australia and the United States.

Research

Research from Manitoba has been cited hundreds of times in Europe, the United States, South America, and Asia. Our findings inform and advance research, clinical care and decision-making including, and beyond, kidney transplantation.

World-class research thrives here.

Professor, Dept. of Internal Medicine, Max Rady College of Medicine, Rady Faculty of Health Sciences at the University of Manitoba, as well as Medical Director of Transplant Manitoba – Adult Renal Transplant Program, and Past Head of the Section of Nephrology in the Dept. of Internal Medicine.

Dr. David Rush

A clinician first and foremost, Dr. Rush's research was the result of a clinical observation, a kidney biopsy with results so poor that he and his team thought this must have been going on for a long time, and there were no other signs of abnormalities.

They began to routinely biopsy all transplant recipients and found that 30% were going through subclinical rejections, rejections that couldn't be detected otherwise.

Across Canada and at leading institutions around the world, people have adopted this technique, which continues to be improved by this team, over time.

"Winnipeg is internationally famous for our clinical work research consortium. But for us, a successful transplant result is most fulfilling, because we know how the transplant benefits the person and we know much more now about how to make that kidney last longer." ***— DR. RUSH***

The Research Team

Winnipeg is home to a team of innovative researchers who have made continuing impacts and contributions to kidney disease research and transplantation. Collectively, this team has extensive knowledge and expertise in clinical experience, research capacity, teaching, knowledge translation, and the ability to attract funding.

Since 1998, five trainees have been mentored under Dr. Rush and Dr. Nickerson. Upon completion of their studies and training, three have remained, Dr. Martin Karpinski, Dr. Juliet Ho, and Dr. Chris Wiebe, gaining enough experience and knowledge to become experts in their own right and developing kidney transplant related research programs. Kidney Pathologist Dr. Ian Gibson joined the team in 2002 and is a key leader, today.

Dr. Kathryn Tinckam and Dr. Stefan Schaub, although no longer based in Winnipeg, remain close collaborators.

DAVID RUSH

PETER NICKERSON

MARTIN KARPINSKI

JULIET HO

STEFAN SCHAUB

KATHRYN TINCKAM

CHRIS WIEBE

IAN GIBSON

Creating our future.

Going forward, the research project will implement another phase of clinical trials, looking to minimize kidney inflammation from the time of transplant, in order to reduce overall subclinical rejection and its resultant injury.

2013

In 2013, the research team studied why patients were forming antibodies. A companion paper on antibodies, the rates of progression once the antibody is present, and the determinants of those outcomes, was published in 2015. The research team remains a leader on post-transplant research.

Currently

The most current research in Winnipeg is routine post-transplant monitoring for patients with antibodies. This has become the new standard of care to be adopted by more institutions of care around the world. This work is about 10 years ahead of similar research in other countries. Due to the unique study in Winnipeg, Dr. Nickerson has taken part in an international consensus report (2013) on behalf of the World Transplant Society.

THE NEW STANDARD OF CARE IS POST-TRANSPLANT MONITORING FOR PATIENTS WITH ANTIBODIES.

THIS HAS BECOME ADOPTED BY MORE INSTITUTIONS OF CARE AROUND THE WORLD.

Transplant Immunology:

> Now, the team is focussing on the role of HLA antibody as a principal determinant of both acute and chronic rejection.

> They are evaluating clinical and pre-transplant factors that determine clinical outcome in renal transplantation.

> Clinical trials are assessing the mechanisms of renal allograft cellular and antibody mediated rejection.

Health Care System Design:

> Using business and engineering tools (Strategy Maps and Balance Scorecards, Process Mapping) the team is developing novel solutions to enhancing access to transplant and improve outcomes for patients with end-organ failure.

> They are developing an organ allocation policy based on translational research, to enhance equitable access to organ transplants.

> They are standardizing laboratory diagnostics policy in Canada to enhance transplant outcomes.

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