

## THE LASER

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## Islet News: an Alliance for Health

You should have been there. It was strategic planning of the highest order.

All the professionals in the room were listening raptly to the protocol for their soon-to-be-first human islet transplant. In a program coordinated by PNRI—HITS: Human Islet Transplantation in Seattle—they were about to test a radical new treatment for type 1 diabetes. In the process they would help advance medical knowledge and improve patients' lives. At the same time, they were demonstrating that an alliance of healthcare researchers could pool their talent and resources in unprecedented ways.

**Good to Go**

Late March, with a heavy afternoon rain. No windows. Thick binders stacked up on a long table.

Dr. Robert Wilburn, a nephrologist and transplant surgeon at Virginia Mason Medical Center, chaired the meeting. Around the table were nurses, ward supervisors, radiologists, endocrinologists, kidney surgeons, research coordinators, and a community relations manager. Wilburn covered the agenda crisply. His decisive monotone conveyed a clear message: "Everybody here understands this. We've been over it many times. But once more, let's make sure. Then we're good to go."

Their talk was almost without any emotional inflection, but beneath its professional austerity, you could hear their excitement.

Everyone's role was defined. Contact numbers were reaffirmed. The transplant timeline was set. How long would it be

from the moment a pancreas became available? How many decision points in the process of isolating the islets? Who would need 10-hour notice? Who'd need 4-hour? When should the patient be called to the hospital? Who would reaffirm patient consent? Checklists? Ward issues? Patient books prepared, with all forms ready to go. Post-op orders?

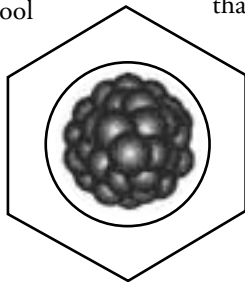
**Islet Transplant Research**

Islets are groups of cells in the pancreas that produce and secrete insulin to control the body's blood sugar. As such, they are key to the disorder of type 1 diabetes. In this disease, the body's immune system turns against the islets' beta cells and destroys them. So persons with type 1 diabetes must get their insulin externally, usually by injection or by an insulin pump.

In recent years, researchers have looked increasingly to transplantation as a way of replacing the diabetic loss of beta cells. Whole pancreas transplantation has been very effective, but it requires major surgery and all the complications and risks that such surgery entails.

Islet transplantation, on the other hand, can be done quickly and easily by a radiologist, inserting the islets through a catheter into the portal vein of the patient's liver.

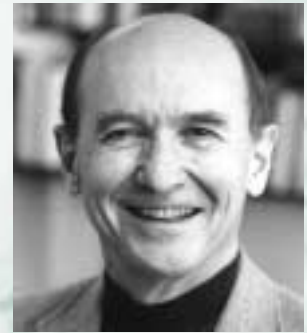
This procedure has achieved success only very recently, and it is now being tested at a number of research centers around the world. HITS is one of those centers. And the thrilling news of this



*HITS: a hexagon with an islet at its center. For more information visit the website [www.pnri.org/hits](http://www.pnri.org/hits)*

## PERSPECTIVES

by R. Paul Robertson, M.D.



## The Dreams of Our Daruma

During the past several years, pancreatic islet transplantation has become almost an obsession for the group of Seattle scientists and clinicians who form the HITS consortium. HITS is the acronym for Human Islet Transplantation in Seattle and includes participants from PNRI, Fred Hutchinson Cancer Research Center, Puget Sound Blood Center, Swedish Medical Center, University of Washington Medical Center, and Virginia Mason Medical Center. We started from ground zero to build the proper laboratory facility, to compete for funding from the Juvenile Diabetes Research Foundation and National Institutes of Health, and to obtain approvals from human subject review committees at three hospitals as well as the Federal Drug Administration.

But now it has happened....three times! During the past few months

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# THE LASER

AUGUST 2002

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FROM THE EDITOR:

## New Light on Giving

by Rich Murphy

One of the most striking moments in a television news special on diabetes broadcast recently here in Seattle occurs when the camera pauses brightly on Jackie Westcott's face.

"Please," she says, addressing the audience simply. "Please."

When that segment was filmed last spring, Jackie was a woman who had had type 1 diabetes for 34 years. Her blood sugar levels had been so erratic for so long, that her kidneys had now failed. She was waiting in line for a kidney transplant and, because she also met the strict eligibility requirements of the experimental trial being coordinated here in Seattle by PNRI, she was also waiting for an islet transplant.

Thus her appeal to the potential donors among us.

As it happens, someone with the right blood type and tissue match had registered to donate their organs, and Jackie has since received both the new kidney and the pancreatic islets she needed to control her diabetes.

But her plea on behalf of the tens of thousands of other patients across the country waiting for donated organs remains starkly eloquent. There aren't enough organs. There aren't enough donors.

So when Elizabeth Kresse, another recent Seattle transplant, got home from the hospital in early June, she immediately

registered herself as an organ donor. "My pancreas won't be any good," she acknowledged, having had diabetes for more than twenty years. Still, as the grateful recipient of someone's healthy pancreas cells, she realized more compellingly than ever before that she has other organs to give.

The immediacy of these stories is unusual for PNRI research. As a general rule, the discoveries of PNRI scientists in immunology, genetics, statistics, and cell chemistry and biology—as critical as they are—are still years away from having immediate effect on the lives of specific patients.

But the effect of islet transplantation research on these patients' lives is compelling today. They feel it, and so does everyone who sees and talks with them. Organ donation takes on new importance in light of their experience.

So, too, do the generous financial contributions of individuals who support the scientific research of PNRI. Their donations are essential to the cancer and diabetes work of Institute scientists. If, like registering for organ donation, they sometimes seem remote from the lives of particular people, if their actual benefits seem somehow far off, listen again to Jackie's plea.

She's looking straight into the camera. She's speaking to us.

*We want you to help us create  
a FUTURE in which  
diabetes and cancer are HISTORY.*

**PNRI**

# Outreach—PNRI Stretches

Literally. On blessedly cool Sunday mornings in May and June, PNRI scientists and administrative staff donned their Institute t-shirts and walked or ran for diabetes and cancer research. In September, another PNRI team will participate in the American Lung Association benefit bicycle ride to Victoria. (If you'd like to join us and ride with Team PNRI, please contact Michael Brantley, by phoning him at the Institute 206-726-1200, or by emailing him, [mbrantley@pnri.org](mailto:mbrantley@pnri.org).)

But we're also stretching out figuratively—cooperating with partner organizations, advancing science education, expanding our presence among regional businesses, and serving the local community. Here are a few examples.

- Vincent Poitout led a team of Institute scientists in creating a scientist-for-a-day program at PNRI. Student winners of the annual Washington Association for Biomedical Research essay and poster contest participated. Along with their teachers and parents, they were guided by PNRI researchers through a series of hands-on laboratory activities typical of professional cancer and diabetes studies.
- PNRI also helped the Washington Association for Biomedical Research to plan its benefit dinner with Nobel laureate Lee Hartwell. Proceeds from the event are earmarked for programs to help teachers advance science education in area schools.

Phuong Oanh Stephan, another PNRI scientist, spent a day at Mill Creek Elementary School, teaching five classes of fifth graders about diabetes. "Exhausting work," she said in amazement, after just the first class. But the children's thank-you letters showed how valuable and effective her teaching was to them. As a follow-up, Oanh is also now contributing to a curriculum guide for teachers on teaching about diabetes.

■ The Institute is working to expand its business presence, too. We participated in Washington CEO's 2002 Best Companies to Work For. PNRI was recognized as one of five non-profit finalists in the state and was featured in the cover story of the June CEO magazine. We also are members of the regional Technology Alliance, an organization of important research, computer, biotechnology, and law professionals, sponsored by the Greater Seattle Chamber of Commerce. In the fall, Paul Robertson, PNRI's scientific director, will address the Alliance's November Roundtable breakfast with an update on islet transplantation.

■ The fall calendar also has three PNRI scientists speaking to a diabetes support group in Kitsap County. As an outgrowth of their involvement in the Diabetes Expo in Seattle in April, Peter Dempsey, Melissa Smith, and Barton Wicksteed have been invited to address a group of diabetes patients at their October meeting. Their topic: the state and promise of stem cell research.

■ Then there's music. Janice Pullman, a PNRI cancer researcher, is also an avid bluegrass fan. On the wings of her enthusiasm, she and Cynthia Jacobs are teaming up with Anna Gottlieb, the executive director of Gilda's Club on Capital Hill in Seattle. Together, they are planning a September 28th bluegrass jam to benefit cancer and diabetes research at PNRI and cancer support programs at Gilda's. If you'd like more information about the concert, or would like to help in any way, please contact Janice by phone at PNRI, 206-726-1200, or by email, [jpullman@pnri.org](mailto:jpullman@pnri.org).

Bluegrass and stem cells? Nobel prize research and bicycle rides? Fifth graders and the Chamber of Commerce? Not so much of a stretch, after all. Just the vital signs of a thriving intellectual center, reaching out.

## PNRI Welcomes New Employees, Post Docs, and Visiting Scientists!

Cari Sutton  
David Scarsella  
Jon Hallstrom  
Kathy Hojjati-Emami  
Kristine Hope  
Larry Taylor  
Levi Jones  
Michael McMillan  
Min-Guy Soung  
Monica Hurtubise  
Naomi Gilman  
Sabrina Andersen  
Shi-Lin Yang



Not shown are David, Naomi, and Shi-Lin.

*In the service of health...*

## Dreams of Our Daruma

*continued from page 1*

we have successfully transplanted islets into the livers of three diabetic patients. As the patients' insulin requirements plummeted, our spirits soared. The question arose: how to celebrate? Being research folks, our ambitions were characteristically modest so we settled for a cake at one of our meetings (covered with rich sugar frosting, of course). But the guest of honor, brought along by Bob Wilburn from Virginia Mason, was a traditional Japanese good luck doll, a daruma.

Our daruma stands four inches tall. It is a face surrounded by a black hood painted with gold stripes. A physical characteristic of the daruma is that it will automatically re-right itself when batted over (seems symbolic of HITS' resiliency). Another traditional feature is its eyes. They begin by being completely empty. The idea is to paint your dreams in the eyes. At the first of our celebratory team meetings, Shinichi Matsumoto of the Blood Center painted one eye to mark the first transplant. When we met to celebrate the second transplant, he painted the second.

Now our daruma is complete, but our dreams are not. We are looking forward to many more of these transplants that provide new hope for patients with diabetes.



## Elizabeth Kresse: Thinking of Others

Elizabeth Kresse is a pro at customer service. For nearly fifteen years, she's been assisting clients and training new employees in California and Oregon to process purchase orders, schedule shipments, and troubleshoot business problems. Now she's working at Pacific Western Pipe in Eugene to give customers the courteous and efficient service they deserve.

She enjoys working with people. She's very good at it. She listens to them, understands what they need, and helps them get it. But Elizabeth has had juvenile diabetes for more than twenty years. And for all her outgoing people skills, she has found diabetes an isolating disease.

"Most people don't understand it," she says. "Those who don't have diabetes don't realize what it's like." They think insulin is a cure. They know almost nothing about the ravaging complications of the disease, little if anything about the terror and danger of hypoglycemia. "Diabetes took away my independence," Elizabeth says. "My boyfriend didn't think I could ever be by myself."

With good reason. Repeatedly in recent years, and without warning, Elizabeth's blood sugar dropped dramatically. Unable to recognize the onset of these episodes herself, she grew irrational, behaved erratically, drove her car recklessly, all in the midst of severe hypoglycemic lows. Only the quick, knowledgeable response of people around her—most often her boyfriend—could protect her from these severe insulin failures.

As the hypoglycemia worsened, Elizabeth became increasingly afraid of the more radical and chronic complications that diabetics face as their years of insulin

dependence are prolonged. And she dealt with that fear, too, in isolation. It was hard to describe the dread, and most of the people she knew—even her family—had little awareness of her experience.

Then, on May 30th, she received the first human islet transplant in the Northwest.

She can't quite believe how lucky she has been to be selected for the HITS research study. She can't yet fathom how simple the islet-transplant procedure was. She's responding to the immunosuppressive drugs successfully, and since her transplant, she has had no severe blood-sugar lows like those that were so fearsome before.

But even as she is celebrating her own good fortune, she's acutely aware of other people. She had been isolated with diabetes, but in her gladness now she thinks immediately of others.

The importance of her transplant isn't limited to her, she told a television interviewer. "It will help others with diabetes, too. This is important," she said. "It will help make a treatment for them that will make their lives better."

She has extended that concern even further. Now that she is the grateful recipient of someone else's pancreas tissue, she wants to become an organ donor herself. The day she returned home to Eugene, she went directly to the DMV office and registered herself as a donor. "It seems the greatest gift of all," she says. "To make somebody's life better. To help them live."

It's just the sort of thing you'd expect from a person whose day job is getting people what they need.



## David Ellis: Counting on Health

David Ellis is in love with numbers. You can tell it in the work he's sought and excelled in. Physics. Meteorology. Electrical engineering. The curves of forces. The clarity and speed of digital signals.

But when the doctors confronted him near his 25th birthday with the shocking news that he had juvenile diabetes, his life became an almost constant struggle with numbers.

"From the get go," he says. Counting, quantifying, sequencing everything. Analyzing his blood sugar. Controlling his diet, what and when and how much he ate. Measuring and scheduling his insulin. He had to coordinate it all, every day. "You tried to make it work as best you could," he says, "but you never got solid control."

And this from a man who helped design the electrical instruments for scanning the fuselages of passenger jets.

The lows were especially difficult for David—the episodes of hypoglycemia, when the count of glucose in his blood shrank so much as to starve his muscles and brain. Such episodes "were so debilitating," he says, "they stopped you from doing anything."

Then the dysfunction of his kidneys. "It was always in the back of my mind that it would come. Suddenly, there it was. They gave out altogether."

Time became a burden too. Dialysis took three hours a day, three days a week. Not counting the additional three hours each time that David and his wife, Marie, spent setting up and taking down the dialysis equipment at home.

The morning of this past June 19, he was working on another number problem. He was in line for a kidney-islet transplant in Seattle. He and Marie were trying to figure out how they could get from their home in Spokane in time if a transplant became possible.

But this time, the numbers were lined up perfectly in his favor. David was already here for a routine visit with his doctors at the University of Washington. A donor kidney became available that morning. By evening a set of pancreatic islets had been processed. By the end of the day, David Ellis was the second successful kidney-islet transplant recipient in the HITS program.

Freed from dialysis. On his way to freedom from insulin.

Just a few weeks after the transplant now, he's still getting used to the anti-rejection medication. But he feels physically very good, better than he can remember for nearly twenty years. The reduction of his insulin requirements and the end of dialysis are, he says, "a great relief." So much so that, as he recuperates here in Seattle, he's working on his laptop computer again, doing electrical engineering research remotely for his eastern Washington company.

He's back to the numbers he loves.

## Jackie Westcott: Goin' fishing

When you ask Jackie Westcott what it was like to have juvenile diabetes for almost thirty-five years, she admits she can't say. She's never known anything else.

Until now.

Diagnosed when she was 7, she's grown up with it, worked with it, lived with it. What's it like to take insulin everyday? She has no standard of comparison. Growing up in small town Alaska, she had three siblings who didn't have diabetes, but it never occurred to her that things could've been different. She didn't always like it, but she never questioned it.

"I was the one who had diabetes. That's just the way it was."

And that's the way it continued for Jackie, all through school and work, as a bookkeeper, a receptionist, an accounts payable clerk, and a bank teller. Currently, she's employed by a heavy equipment construction company that builds roads and installs water and sewer lines in and around Petersburg, Alaska. For the last year and a half, as a complication of her diabetes, she's been without functioning kidneys.

Now that's been hard, she admits readily. Diabetes? "I don't think it's terribly bad," she says. "I mean, I know I could have had something much worse. Or something that I'd say was worse. But the kidneys . . ." Her voice trails off into silence.

Seven days a week. Four peritoneal fluid exchanges a day. First thing in the morning before work. Then home for lunch and another exchange. Back to work for the afternoon, then home for a third exchange, dinner, the dishes, a last exchange, and bed. It was a life in which Jackie could hardly ever get to work on time, one in which besides work and dialysis, she was able to do practically nothing.

So what's it like now, in the first weeks after her kidney-islet transplant? "GREAT," she says, giving the word exaggerated emphasis. "It's absolutely WONDERFUL." And then, her voice trailing off into silence again, she adds, "I can't even describe it."

Pause, and the thought comes rushing back to her, with her life. "I can go fishing again."

*join us in discovery...*

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## PNRI PRINCIPAL INVESTIGATORS and their major areas of research

- Peter Dempsey, Ph.D.  
*(Cellular communication, ErbB ligand trafficking and processing, disintegrin-metalloproteases, ErbB receptor signaling)*
- William A. Hagopian, M.D., Ph.D.  
*(Type 1 diabetes mellitus)*
- Senitiro Hakomori, M.D., Ph.D.  
*(Aberrant cell recognition and signaling in cancer, based on changes in glycosylation)*
- Ingegerd Hellström, M.D., Ph.D.  
*(Tumor immunology)*
- Karl Erik Hellström, M.D., Ph.D.  
*(Tumor immunology)*
- Michael Kahn, Ph.D.  
*(Chemical biology & functional genomics)*
- Jeffrey A. Ledbetter, Ph.D.  
*(Cancer immunotherapy and T cell tolerance in autoimmune disease)*
- Donald Malins, Ph.D., D.Sc.  
*(Breast, ovarian, prostate cancer)*
- Vincent Poitout, D.V.M., Ph.D.  
*(Pancreatic beta-cell dysfunction in Type 2 diabetes)*
- Christopher Rhodes, Ph.D.  
*(Biochemistry of pancreatic beta cells)*
- R. Paul Robertson, M.D.  
*(Pancreas and islet transplantation, glucose toxicity of pancreatic beta cells)*

PNRI

## Islet News: an Alliance for Health

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summer is that HITS has transplanted the first three of its patients here in Seattle.

First, Dr. Robert Wilburn's team at Virginia Mason Medical Center successfully transplanted Elizabeth Kresse. Not two weeks later, the transplant team of Dr. William Marks at Swedish Medical Center performed an islet transplant on Jackie Westcott. This time, the islet procedure was performed in conjunction with a kidney transplant, a combination being pioneered by the HITS group. Another kidney-islet transplant was then performed on David Ellis at the University of Washington Medical Center, under the direction of Dr. Christopher Marsh.

### A Model of Institutional Teamwork

Chris Marsh is the associate director of the transplantation program at the University of Washington. He calls HITS a model. "We've brought multiple institutions together," Dr. Marsh says, "to share their resources and expertise. To combine their strengths to work on a common problem. This is a model other research centers around the world can adopt. We're flying all our flags together."

Marsh's enthusiasm is shared by researchers from other HITS institutions.

Right now, there's no more exciting place in the world for diabetes research than Seattle. A constellation of important study centers is located here. Among them are PNRI, the Puget Sound Blood Center, the Fred Hutchinson Cancer Research Center, as well as sites that combine research and clinical practice like Swedish Medical Center, Virginia Mason Medical Center, and the University of Washington Medical Center.

For the past three years, PNRI has been playing a pivotal role in bringing these important institutions together in cooperative research. The most visible product of its leadership is the Juvenile Diabetes Research Foundation Center for Human Islet Transplantation in Seattle.

When asked about their hopes for the collaboration, HITS members have answers that come understandably from their different perspectives. According to Margery Moogk of the Blood Center, one of the most important facts about islet transplantation success is the generosity of the organ donors who make it possible. Swedish surgeon Bill Marks emphasizes the sober, deliberative view: that for all its importance and promise, islet transplantation must be seen as still evolving. Chris Marsh expresses his gladness for the patients. "At last it seems possible," he says, "for very sick people to have hope of a cure."

But these and others in the HITS consortium all agree that their cooperative success so far—and their promise of fruitful future collaboration—are due in large part to the leadership of PNRI Scientific Director Paul Robertson. As HITS project director, Robertson has guided and facilitated the team. And they are all proud of their joint accomplishment.

So the news they are reporting this summer has two success themes. First, that their talent, energy, and expertise are bringing a cure for type 1 diabetes closer. And second, that with patience, professional modesty, and institutional cooperation, they have together created a remarkable scientific partnership.

*"This is a model other research centers  
around the world can adopt.  
We're flying all our flags together."*



PROFILE:

# In Pursuit of Hope

Linda Bonomi, the new Director of Development at PNRI, is coming home to Seattle where her development career began.

Energized by years of fund-raising success at a number of non-profit health-care institutions, Linda is thrilled to be joining PNRI. "It's a stellar organization," Linda says. "When you say its name, everyone knows. Its excellence is obvious." And what could be better, she asks with lyrical enthusiasm, than helping to make health possible?

Linda didn't start out to be a development officer. Nor was Washington originally her home.

A rural North Dakota child, Linda grew up with parents who served. Her father was a school teacher; her mother a health care professional. Linda, the oldest of five kids, was given a lot of responsibility at home and discovered early on that she could successfully manage household tasks, school work, and extracurricular activities using her natural talent for organizing.

So it was little surprise that she found herself coordinating conferences at the MultiCare Medical Center in Tacoma, or leading teams of fund-raising volunteers in the new Seattle office of City of Hope, or creating a corporate giving program for the

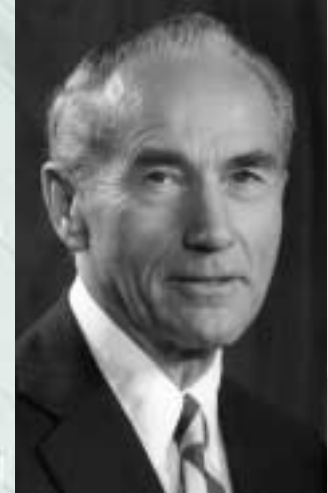
Fred Hutchinson Cancer Research Center. (The irony is not lost on her, that she is now going to be working on behalf of the first and oldest scientific research institute Bill Hutchinson started.)

But her eyes are fixed on more than science or financial gifts. Her goals are always people-oriented. She's a relationship-builder. She's a lobbyist for patients who need science to live.

It doesn't hurt that she has fun doing it, that she was a drum majorette in high school, that she thinks of life as an "adventure," and that the catalog of things she loves is too long to list. (Hint: it includes three grandchildren, the youngest just two weeks old.)

What will she say when you ask her about PNRI, now that she's back from work in Southern California with the Eisenhower Medical Center and the American Cancer Society? Well, it'll be about excitement and opportunity, about scientific excellence and hope. About how the millions of people with diabetes and cancer deserve no less.

But here's a suggestion. Rather than take our word for it, give her a call at the Institute (206-726-1200). She wants to tell you herself.



## Remembering Dr. Hutchinson

Bill Hutchinson was a pioneer in medical research. He founded PNRI in 1956 as one of the Northwest's first non-profit institutes and began the Fred Hutchinson Cancer Research Center in 1972 in memory of his brother.

A whole host of companies including Immunex, Seattle Biomedical, and ICOS have arisen because Bill Hutchinson had a vision that private research could enrich and improve human life.

PNRI continues that vision today in pioneering studies of cancer and diabetes.

The Dr. William B. Hutchinson Research Fund offers an opportunity for you to further this work. Contributions may be made by sending them to the Hutchinson Research Fund at PNRI, 720 Broadway, Seattle 98122. By calling 206-726-1200. Or by emailing [support@pnri.org](mailto:support@pnri.org).

## Institute Kudos

Several PNRI scientists have recently been awarded new and continuing grants to support their research.

■ **Peter Dempsey** received a three-year grant from the Juvenile Diabetes Research Foundation. This grant will fund his study of ErbB receptor signaling in beta cell growth and differentiation.

■ **R. Paul Robertson** received four-year renewals of two grants from the National Institutes of Health. The first grant supports the study of glucose regulation of pancreatic islet gene expression. The second funds further study of pancreas and islet transplantation in humans.

■ **Vincent Poitout** received a five-year career development award from the American Diabetes Association. This award will enable him to extend his research into the mechanisms of stimulation of insulin secretion by fatty acids.



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# THE LASER

AUGUST 2002

## PNRI MISSION STATEMENT

The mission of the Pacific Northwest Research Institute is to prevent and cure cancer and diabetes and thereby help relieve human suffering.

Visit us on the web at:

[www.pnri.org](http://www.pnri.org)

## HISTORY

# A Note on Early Transplantation Science

In the last decade of the nineteenth century, P. Watson Williams, M.D., Senior Assistant Physician of the Bristol Royal Infirmary, reported what may have been the first attempt to use transplantation as a treatment for diabetes. Writing in the *British Medical Journal*, Dr. Williams recounted how he attempted to transplant pancreas tissue into a young diabetes patient in the hope of controlling the patient's blood sugar. The operation was not successful, but Williams' account of it shows that more than a hundred years ago scientists were exploring the possibility that transplantation might help manage, even cure diabetes. In the light of recent successes with pancreatic islet transplantation here in Seattle and elsewhere, Williams' paper provides a fascinating glimpse into the slow, complex progress of science.

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*"No disease [Williams wrote in 1894] has received a larger share of attention at the hands of clinicians, pathologists, and chemists in the last fifty years than has diabetes, while the ample literature and the very diverse opinions that have been advanced by the most able observers in regard to its pathology and treatment testify to the difficulties which surround us when we seek to explain the problems involved. Certain facts recently come to our knowledge seem at first sight to justify very important conclusions as to the real nature of diabetes, and to indicate fresh lines of treatment as at least affording some chance of increased control over this disease."*

—from "Notes on Diabetes Treated with Extract and by Grafts of Sheep's Pancreas."  
*British Medical Journal* 1894(2): 1303-1304.