

# TRAVERSING A TIGHTROPE OF TREATMENT

by LISA SPELLMAN



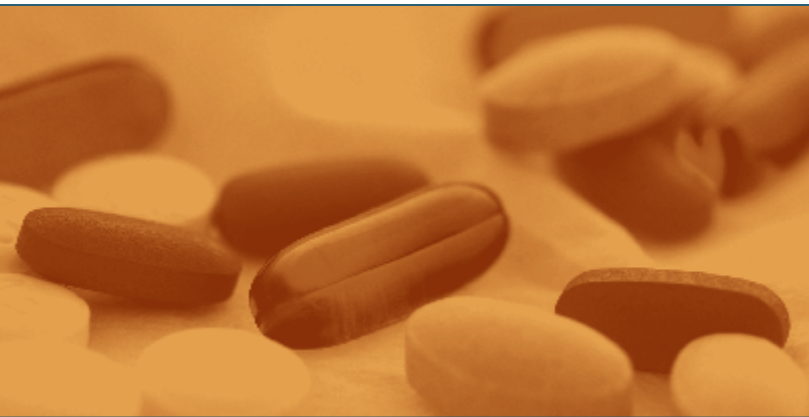
KEA HUQ KNEW IT WOULD BE A BALANCING ACT AFTER HER KIDNEY TRANSPLANT IN 2004.

On one hand she felt better than she had in years, on the other she would forever be forced to take powerful medications to keep her body from rejecting the donated organ.

One risk she didn't count on was

developing diabetes because of those medications.

With more than 97,000 people on the waiting list for an organ transplant, Huq (pronounced 'Huk') considered herself lucky to receive a new kidney.



“WHILE GENETICS PROBABLY PLAYS A ROLE IN THE DEVELOPMENT OF DIABETES AFTER TRANSPLANT, IMMUNOSUPPRESSANT DRUGS MAY PUSH INDIVIDUALS AT RISK OVER THE EDGE IF THEY CAN CAUSE INSULIN RESISTANCE, TOO.”

JENNIFER LARSEN, M.D.



KEA HUQ

## UNMC seeks national recognition as ‘bench to bedside’ leader

UNMC is striving to become a national leader in clinical and translational research in the areas of cancer, transplantation, biopreparedness and neurosciences. The academic medical center hopes to secure one of the 60 Clinical and Translational Science Awards (CTSA) from the National Institutes of Health.

In November, the NU Board of Regents approved the establishment of the Center for Clinical and Translational Research in an attempt to strengthen the pending application. UNMC plans to apply for the CTSA award in October 2008.

The comprehensive center will provide an administrative structure, improved training, space and core facilities to support clinical and translational research across all four UNMC campuses. Collaborations with underserved communities also will be developed.

The advent of this new award is part of a national movement to create a stronger health care system by transforming clinical and translational research at academic health centers across the country.

NIH officials created the awards to increase collaboration between researchers from differing disciplines, making the translation of research from bench to bedside more efficient.

Improved interactions between scientists, clinical practitioners, behavioral specialists, biostatisticians, epidemiologists, bioengineers, pharmacologists, medical economists, community members and patients may be key to solving medical mysteries, said Jennifer Larsen, M.D., associate dean for clinical research, UNMC College of Medicine.

Dr. Larsen said UNMC hopes to receive a CTSA by the time the award process is finalized in 2012. In preparing to apply for a CTSA, Dr. Larsen’s team has been re-evaluating UNMC’s clinical and translational research enterprise. Some of the new developments out of this process include the initiation of a new research-training track that allows different health care professionals to learn the latest clinical and translational research technology side-by-side. Other developments include a universitywide clinical and translational research seminar for both clinicians and basic scientists and exploring new ways that investigators with common research interests can meet and collaborate.

“UNMC has many resources in place that make securing a CTSA possible,” Dr. Larsen said, “including new research facilities, multiple areas of established translational research expertise, an electronic medical record and considerable expertise in the areas of health informatics and bioinformatics.” Even so, she said, there is much left to do to improve collaborations across disciplines, as well as with neighboring institutions.

“I was so glad to be alive,” Huq said. But, her happiness would turn into anxiety a year after her transplant when the Douglas County Hospital charge nurse was diagnosed with diabetes.

Roughly 25 percent of transplant patients develop diabetes after their life-saving operation.

Jennifer Larsen, M.D., associate dean for clinical research at UNMC, is working to prevent this treatment complication.

In 2006, Dr. Larsen published a study in the journal “Transplantation” that provides evidence to support her theory that the immunosuppressant drugs tacrolimus and sirolimus, known by the trade names Prograf® and Rapamune®, cause insulin resistance.

“It was widely believed that corticosteroids, such as prednisone, one of the most common anti-rejection drugs, was the main cause of insulin resistance and diabetes after a transplant.

“Considerable effort was made to find immune suppressant regimens that didn’t require corticosteroids that would still be as effective. Often those regimens included tacrolimus or sirolimus, but post-transplant diabetes wasn’t reduced,” she said.

Dr. Larsen began to wonder if these two immunosuppressants could be the culprit and in 2004 began testing her theory in male rats.

“After just two weeks of daily injections of either drug, the normal rats began to have elevated blood sugars,” she said.

More importantly, Dr. Larsen discovered that treatment with sirolimus resulted in higher blood insulin levels, even more than the tacrolimus.

“This is similar to what occurs with insulin resistance that leads to type 2 diabetes,” she said.

Now, Dr. Larsen wants to understand how these two important anti-rejection medications cause insulin resistance.

“If we can discover the mechanism, maybe we can tailor new immune suppressant drugs that are less likely to cause diabetes or develop therapies to prevent diabetes in transplant patients,” she said.

Huq, who received her transplant at the Mayo Clinic in Minneapolis, appreciates Dr. Larsen’s commitment to finding a way to prevent diabetes in people who already have gone through so much.

“These anti-rejection medications are so powerful, I wish more doctors would be careful,” Huq said.

But without the medication Huq’s body would reject the new organ.

While post-transplant diabetes can occur after any transplant, the current numbers are generally lower after a liver or heart transplant than after a kidney transplant, Dr. Larsen said.

Many factors contribute to these differences, such as the age at which the individual has the transplant, their individual risk factors for developing diabetes, such as weight and family history, as well as which medications are used, she said.

“While genetics probably plays a role in the development of diabetes after transplant, immunosuppressant drugs may push individuals at risk over the edge if they can cause insulin resistance, too,” Dr. Larsen said.

And patients who develop insulin resistance and diabetes after transplant seem to require insulin for treatment sooner than individuals who develop diabetes who’ve never had a transplant.

That’s why Dr. Larsen and other diabetes physicians work closely with the transplant team at UNMC to evaluate

patients before and after they receive a kidney, pancreas or islet cell transplant.

Patients who receive a kidney, pancreas or islet cell transplant are screened for elevated glucose levels at every visit – at least four times the first year following their transplant and at least once a year thereafter.

Dr. Larsen credits James Lane, M.D., an endocrinologist at UNMC who works closely with the transplant team, with discovering that if transplant patients are going to develop diabetes, they are most likely to develop it in the first year after their transplant.

And so it was for Huq, who began to notice her blood sugar numbers rise within the first few months after her kidney transplant.

“When I first noticed it my blood sugar was 120,” she said. “My doctors suggested I change my diet to try to control it, but it continued to rise.”

Normal fasting blood sugar is less than 100. Fasting blood sugars between 100 and 125 are now recognized to represent pre-diabetes, which suggests diabetes could be developing and fasting blood sugars of 126 or greater is the level at which diabetes is diagnosed.

When her blood sugar hit 160, Huq sought out a doctor closer to home to help control her blood sugar.

Huq is now followed by Dr. Lane. She has her lab work done at UNMC and sent to her doctors at the Mayo Clinic.

So far, Huq only has had to take medications to help control her diabetes.

While she has not had the easiest time since her transplant, Huq said she would do it all over again if she had to, with one exception.

“I would want to know more about the medications and talk to the doctors about trying to find the best combination so that, hopefully, I wouldn’t develop diabetes,” she said. 🍷