Doctor of Mice

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Thud!

Five-year-old Iris fainted when she saw the mice inside our rickety car. But the mice themselves were at fault. They were quite cute, with white furry coat, curious eyes and orange-brown tails. Each of them had arrived in separate ventilated cages all the way from the Jackson Laboratory in the United States.

Unlike my daughter, I was thrilled to meet them. The Jackson mice were famous. In fact, they were revered as if they were rock-stars of the animal kingdom (like their namesake Mr. Michael Jackson). Journal after journal screamed headlines about them in the scientific world. Their specialty was that they naturally developed diabetes, like some of us humans do.High glucose levelsin these mice mimicked this disease.

Diabetes is a troublesome disease. In fact, there are two types, and the more common type of diabetes affects adults. In our community we have an uncle who looks mucholder than he actually is. He takes 12 different kinds of tablets daily. It turns out that he is a diabetic and takes doses of insulin injections too. Each day, insulin is produced normally in the body when we take our meals. The more glucose we consume, the more insulin our body synthesizes. Highly specialized cells in the human pancreas, thebeta cells, are our factories that manufacture insulin. The scientists, Banting and Best, discovered this hormonea 100 years ago. Now commercial insulin is available in syringes and vials.

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* Ms. Neenu Jacob, Ph.D. Scholar from Post Graduate Institute of Medical Education & Research, Chandigarh, is pursuing her research on "Suppression of Type 1 Diabetes in Non Obese Diabetic (NOD) Mice by the Induction of Colonic Regulatory T Cells." Her popular science story entitled "Doctor of Mice" has been selected for AWSAR Award.

A particularly vicious type of diabetes affects kids. The immune system in these children mistakenly attacks the beta cells. The beta cells die and disappear. So instead of playing around in the parks, children who have diabetes inject themselves with insulin. They become smaller in size compared to other children. Insulin is a lifesaver for many of them, but a large dose of it could kill instantly. Thousands of children die each year with diabetes and its complications.

My thesis was founded on the premise that our habits of daily life play a crucial role in the progression of diabetes, specifically diet. It is common knowledge that the Indian diet has changed inmodern times. We now have many children eating processed and ready-to-eat food. These changes automatically lead to disturbance in the intestinal bacteria. There is good and bad bacteria in our intestines. Science tells us that commensal bacteria are our friends and they help us. These are the good bacteria. They feed on dietary fibre and generate short-chain fatty acids. Fast food, poor infibre, changes the bacterial flora of our intestines. The short-chain fatty acids are of vital importance to the local immunity. One of these short-chain fatty acids is butyrate. Sodium butyrate increases T cells in the intestines. These T cells are the guardian angels of our immune system. Their presence tones down and quells the immunological battles that the human body regrettably wages on its own cells. This is called immune tolerance.

Both pancreas and intestines are closely connected, like my husband and me- married to each other; made for each other. As per my logic, the same immune cells patrolling the intestines extended to the pancreas. But science demands proof of such ideations. So the mouse pancreas had to be explored for the presence of T cells. Plenty of T cells meant that the beta cells would be protected from the immunological hara-kiri of diabetes.

The Jackson mice developed diabetes over several weeks. I fed them a special diet, looked after their water intake and otherwise set them free to, well, socialize. What I needed to find out was the

changes in their pancreas, those glands that produced insulin. For this, at regular intervals, the mice came to me for a blood and urine check.

For years, I watched the mice in two animal facilities in our city. One was an advanced lab, dedicated to breeding them. And then I transported them to the lab in the hospital. I monitored their glucose levels by withdrawing blood from their tails.

Some of the mice were like those children taking insulin. They were sluggish and lethargic. The polar opposite of the garden variety of mice, which scoot the moment you look at them.

I administered sodium butyrate mixed in drinking water to the Jackson mice. This was performed after the mice were confirmed to have high glucose levels in the blood. I followed up their blood glucose levels, keeping them on a regimented diet. The blood check-up continued for several weeks. I hoped sodium butyrate would decrease their blood glucose levels. But it turned out to be more complicated than I had anticipated. The mice got pregnant and gave birth to second, third and fourth generations. Many of them turned diabetic while they were pregnant. Their glucose values fluctuated considerably. For many months, I simply collected data; I could not make any sense of it.

My husband is a surgeon. He couldn't quite believe when I told him I needed a pair of the surgeon's scissors. Instead of chopping vegetables in the kitchen, I cut out the pancreas in the lab. No more curry masalas. In their place, I mixed solutions to identify immune cells under a microscope. And instead of sipping coffee in the balcony, my disgruntled husband waited in the car for the lights to dim in my lab.

As a next step, the mouse pancreas were viewed under high power magnification. We used red and blue colour dyes on glass slides. In a sense, the pancreatic glands were dressed up and photographed. We found intact beta cells in these pictures. Further, I measured the percentage of T cells in the intestines and the pancreas. This was achieved with the help of flowcytometry, a new tool to measure microscopic amounts of intestinal lymphocytes. The increased percentages of T cells showed that sodium butyrate could bring about immune tolerance.

My study pointed out that addition of fibre in diet favorably influences insulin. The progression of diabetes can be controlled. A diet enriched in fibre results in alterations at even the cellular and microscopic level.The effects that I found in mice may change a diabetic child's future tomorrow. My experiments over five years also taught me that managing diabetes is a continuous process. It has its ups and downs. It requires time, dedication, discipline and patience. Just like my work in my lab.

My daughter Iris just started kindergarten. She is a chatterbox. The other day, my daughter's class teacher asked her what her parents did. My daughter replied that her father is a doctor of operations andher mother is a doctor of mice!