Trial to Reduce IDDM in the Genetically at Risk

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TRIGR Family News

EDITOR'S CORNER

Dear Study Families!

The TRIGR Study Doctor Alar Abram, who works at Kanta-Häme Central Hospital in Hämeenlinna, Finland, wrote an interesting article about the history of insulin. The Shirt story tells about a very brave young man doing his annual TRIGR Study visit and the Canadians tell about dietary trends and offer us funny apple rings.

The children in our study are now between 3 and 7.5-year old, and the study is proceeding very well thanks to all of you Study Families. I emphasize how important it is to attend the annual Study Center visits in order to get reliable answers to the questions that we are asking.

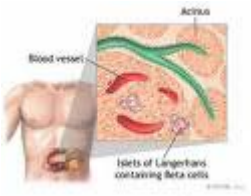
Matti Koski
Chief Editor

The story of insulin

Disease diabetes is known for thousands of years. First time it was described in the ancient Egypt papyrus dated 1500-3000 years BC. The term Diabetes Mellitus was used first time by an ancient Greek doctor **Aretaeus** in the second century. Diabetes is the Greek word for tube because nutrients begin to pass through the system rather than being utilized. Mellitus is a Latin word for honey.

When the medical student **Paul Langerhans** pointed his microscope to the structure of the human pancreas in the University of Berlin in 1869, no one (even the 22-year-old Paul himself) had any idea about the connection between the pancreas and diabetes. In February 1869, he presented his thesis entitled "Contributions to the microscopic anatomy of the pancreas", in which he refers to islands of clear cells throughout the gland, staining differently than the surrounding tissue. He noticed that these areas were more richly innervated, but he could not suggest any function for them, except for the incorrect hypothesis that they might be lymph nodes. These islands were later named the islets of Langerhans.

Paul Langerhans



Islets of Langerhans

The next step in the invention of insulin took place 20 years later. In 1889 the German scientists **Oskar Minkowski** and **Joseph von Mering** were making experiments on dogs during their studies on the role of the pancreas in the metabolism of fat. A few days later when the pancreas had been removed from the dog, the dog-keeper noticed that hordes of flies gather around the urine of that dog. When the researchers studied the urine it was rich in sugar. Then they re-transplanted pacreatic tissue under the dogs' skin and the disease disappeared. Because of the decay of the exocrinic pancreas due to the absence of a duct after such a procedure, they proposed that diabetes was caused by internal deficiency of a substance excreted by pancreas into blood.

Oskar Minkowski

Josep von Mering

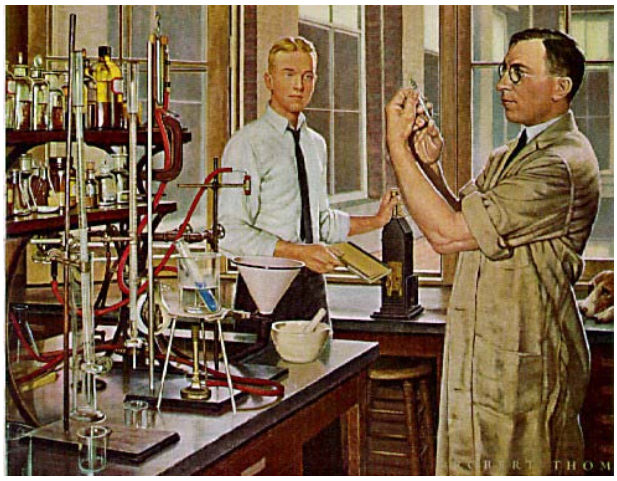
In 1893 **Édouard Laguesse** proposed that diabetes was caused by the absence of the substance produced by the islets of pancreas.

In 1901 another major step was taken by **Eugene Opie,** a medical student atJohn Hopkins University in Baltimore. He noted that there was a connection between beta-cell destruction and deaths. He clearly established the link between the islets of Langerhans and diabetes.

At the beginning of the 1900's many scientists were working intensively to find an antidiabetic hormone. In 1909 a Belgian researcher **Jean de Meyer** named this hypothetical hormone insulin.

In the field of inventing insulin the German researcher **Georg Ludwig Zuelzer** from Berlin achieved results. In 1906 he managed to deactivate digestive enzymes and then after alcoholic extraction he obtained a solution that maintained the urinary sugar levels of a rabbit under control without pancreas. Three years later he injected his extract under the skin of a comatose 50-year-old diabetic patient in a private clinic in Berlin. The next day he injected another 10cc. The overall condition improved, the patient's appetite returned and severe dizziness disappeared. There was, however, no more extract and the patient fell into coma and died. Dr. Zuelzer named his pancreatic extract Acomatrol. He injected it to diabetic patients and reported some improvement, but not in all cases because of side effects of the solution. Even though trying hard he never succeeded to purify his solution sufficiently.

Nicolae Paulescu at the University of Bucharest was among those who tried to isolate insulin. He managed to prepare an aqueous extract of the gland that proved to be successful in diabetic dogs, but due to the World War I he had to stop his experiments until 1919. In 1921 he reported a successful isolation of the antidiabetic hormone which he named pancreine.



A Canadian surgeon

The culmination of all the studies was the epoch-making discovery of insulin in the summer of 1921 at the University of Toronto where professor **J.J.R Macleod** gave his laboratory for the whole summer to **Dr. Frederic G. Banting** and **Charles H. Best,** a graduate student in physiology. They had accepted as the working hypothesis that the islet cells produced an internal secretion which was essential to sugar metabolism. Banting, a young surgeon, got this idea from **Moses Barron** who described in 1920 that blocking of the pancreatic duct by a stone resulted in evanescence of digestive pancreas, but complete preservation of islets and no diabetes. Professor Macleod himself perhaps was not very hopeful about the experiments of the young men and set off to his summer vacation of grouse shooting in Scotland.

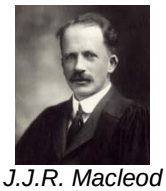
Banting and Best set out to work to prove their hypothesis by extracting the active substance and demonstrating its efficacy in reducing blood sugar concentrations in diabetic animals. The role of Best became invaluable, since he acquired a good technique for blood sugar determinations. When Macleod returned from vacation, he had to admit that the young men had been very successful in extracting the solution that cured diabetic dogs. The proof that their extracting technology was satisfactory encouraged them to work day and night until the winter injecting dogs with extracts prepared by a variety of methods. In December of 1921, when Banting and Best were having difficulties in refining the pancreatic extract, MacLeod freed the biochemist **James Collip** from his other research activities to enable him to join the research team. His task was to purify insulin. Within a month Collip achieved the goal of preparing a pancreatic extract pure enough to be used in clinical trials. The culmination was reached during the Christmas vacation when they injected each other with their extract. No other side effects, than some redness at the injection site, were observed.

Then they began the tests on the patients. The solution was named insulin, and two individuals received the first insulin shots. The first was Dr. Joe Gilchrist, a young diabetic physician who began insulin treatment experimentally and gave the first description of hypoglycaemia experienced after the injection. He was called the "human rabbit". The second was Leonard Thompson. With an injection on January 11, 1922, his blood sugar fell and he survived 15 years on insulin until he died in 1937 at the age of 29 in a motorbike accident.

Controlling diabetes

The insulin solution developed in Toronto was so effective and pure that hundreds of patients got help. Already in 1922 the manufacturing of insulin started. An adverse effect of the success was that the supplies ran out and some of the patients died. Subsequently the information of the purification technique was delivered to other laboratories and companies and a real mass production began.

Frederick G. Banting



J.J.R. Macleod

Charles H. Best

In 1923 Banting and Macleod were rewarded the Nobel Prize in physiology. Banting shared his portion of the prize with Best to express dissatisfaction with his colleague being overlooked by the Nobel Prize Committee and Macleod shared his portion with Collip.

Alar Abram, paediatrician, diabetologist,
Kanta-Häme Central Hospital

The Shirt Story

We all know how hard a blood draw can be for a child but do we ever think how hard it is on the parent. This story is from a mother who is enrolled in the St Louis site in the United States. It is a funny tale about taking her 4 year old for his annual blood draw.

* * *

I have found that the 4-5 year old age group has been a little challenging when it comes to drawing their blood but their perspective on the world is amazing.

Our soon to be 4 year old son was determined **NOT** to participate in this year's TRIGR blood draw. I have been talking to him about it for a week now. I told him how brave boys are able to sit still, etc. I even talked about possible treats following the blood draw.

In the past, every blood draw ends with drama. Today, I knew we had to go to the lab. I opted not to tell him where we were going until we arrived. I knew we were going to a "new" location, so he didn't catch on at first. When we parked, he asked me if we were going to the hospital. At that point, I had to tell him the truth. He quickly jumped over the back seat of the van and would not get out. I had to physically remove him from the vehicle. I'll just say we had hysterics. Just use your imagination! He kept yelling at the top of his lungs, "I don't want to get my blood draw."

We walked, (OK, me carrying the distressed patient), into the lab 3 times. I tried to grab a number to register but I had an escapee. We tried again and didn't get much further. Finally, an employee brought me the sign in pad, took the vials and the order. I decided to take him outside for a walk. Soon there was a knock on the window. The same employee motioned for us to come back in and follow her to the lab. It did take three tries to get him back in the door!

The lab tech did the stick despite the fact my son never quieted. It only took one attempt. The lab tech was awesome. My son finally stopped crying in over 15 minutes. Except for the drive to and from the lab, it was really fast.

I can only hope as he gets older, we can do this without him freaking out too much. Did it hurt? Probably not as much as he feared.

My son enjoyed a chocolate doughnut on the way home. It is likely he won't remember how distressing it all was but I know I'll never forget. Makes me question my decision to do this for 10 years! The blood samples are on their way.

I have to add the funny parts now. When my son got his new "birthday shirt", he was so excited. I suggested he not wear it until his birthday but that was too long for him to wait. So I suggested he wait until his "birthday" month. As soon as October 1st came, he knew what he wanted to wear.

Today, at the hospital, he kept yelling, "Mail my shirt back. I don't want to do the blood draw". I think he gets the connection between the birthday shirt and the blood draw.

When we returned home, he promptly found his "birthday" shirt in the dirty clothes basket and put it on. He now talks proudly about his trip to the hospital.

The story of the TRIGR-family's mother edited by Margaret Franciscus
USA TRIGR Project Manager

Dietary Trends of Canadian Children

In general, the families in our region are health conscious and most families consume whole grain/dark breads and choose fresh fruit over juice. In fact the majority of the children prefer to drink water to fruit juices.

Although the children eat a well balanced diet, they are flexible to include "treats" such as cookies, granola bars. Many of the children are school-age and bring something to school to have along with lunch. The average is 4-6 times per week. Even though it is not on the food frequency questionnaire, when asked about "other milk products" (i.e. chocolate) almost all moms (parents) voluntarily reported that the children do not get sugary candy. Most often, the preferred snacks are crackers, cheese or fruit.

The children appear to be meeting Canada's Food Guide recommendations for dairy products by drinking milk 1-2 times per day and eating cheese. Half consume regular yogurt and/or frozen yogurt 1-3 times per week. This may have something to do with seasonal intake as the most recent interviews included summer months.

Overall, the parent interviewed felt that the child had a good appetite and ate enough variety from all of the food groups. For those who had a "picky eater" most gave a Children's multivitamin supplement.

Submitted by:
Tammy Cooper, RD, CDE
TRIGR Dietitian, Ottawa, Canada

Funny Face Apple Rings

As our children grow, so does their interest in food and preparing their own snacks. Here's a snack kids (and parents) of all ages can enjoy making. Not only can children use their imagination creating funny faces and crazy designs on these healthy apple snacks, they can choose the toppings they like and have fun eating fruit!

Ingredients:

2 large apples (hard green apples work best)
8 tbsp. (100 ml) peach flavoured soft cheese (or any other preferred fruit flavoured cheese)

Suggested toppings for decorating apples:
Dried cranberries
Dried cherries or blueberries
Raisins
Currants
Diced dried apricots
Sunflower seeds
Favourite nuts
Shredded coconut

Directions:

1. Cut each apple into 4 slices horizontally. Discard the top and bottom piece. Use a paring knife or melon baler to remove the core in each of the two remaining pieces.
2. Spread each apple slice with 1 tbsp (15 mL) of cream cheese.
3. Let your kids decorate each slice with the toppings.

Nutritional information per serving:

(2-apple rings and 2-tbsp/25 mL cheese)
Calories: 115
Protein 3 g
Fat 6 g
Carbohydrate 14 g
Dietary fibre 2 g

Brenda Bradley/Tammy Cooper Ottawa, Canada