

# New Drugs that Have Changed Healthcare

## 1. Insulin

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### ■ What is Insulin?

Have you ever heard the word, “insulin”? Insulin is a hormone that is secreted by beta-cells, which are located in aggregations of cells in the pancreas, known as the islets of Langerhans.

We humans need energy to do activities, and the source of this energy is glucose. Glucose is produced when carbohydrates contained in foods are digested and degraded in the body. It is then absorbed through the intestinal wall and enters the blood.

The concentration of the glucose in the blood is called the blood sugar level. The glucose in the blood enters cells of muscles and organs and is used as an energy source. In the liver, glycogen is synthesized from glucose and it is stored. The glycogen, which has been stored in the liver, is degraded into glucose and released in the blood circulation whenever energy is needed.

When the blood sugar level rises, insulin is secreted in the pancreas. It promotes glucose uptake by cells and glycogen synthesis in the

liver. Therefore, if insulin is not secreted at all or if the amount secreted is not adequate, or if the body does not respond to insulin, even though it is secreted, the blood sugar level increases. A high blood sugar level indicates that energy is not delivered to muscles and organs. When this condition is prolonged, diabetes mellitus develops.

### ■ What is diabetes mellitus?

According to a 2007 survey, there are 8,900,000 diabetes patients in Japan. So, someone you know may also have diabetes.

Diabetes mellitus is called “Tonyo-byo (Sugar urine disease)” in Japanese. What a weird name! People call this disease “Tonyo-byo” because, when the blood sugar level increases, sugar is secreted in the urine. According to old Chinese literature, they used to take patients’ urine in a small plate and made a diagnosis of diabetes if it attracted any ants. Thus, diabetes has been known for a long time. There is a description of this disease in Egyptian literature from 16 B.C., and it used to be known as

“kawaki no yamai (sickness of thirst)” or “kachi no yamai” in the Heian era in Japan.

Diabetes patients develop such symptoms as thirst; a need to go to the toilet frequently to pass urine; a strange smell of their urine; their wounds take a long time to heal. They develop eruptions easily, and also develop muscle cramps in their legs, feel sluggish, become tired easily, and lose weight even if they have been eating well. These symptoms appear when diabetes is aggravated and the blood sugar level becomes very high. In other words, the majority of people whose blood sugar level is just slightly increased, do not develop such symptoms at all.

### ■ Types of diabetes

There are roughly two types of diabetes mellitus: Type I and Type II. The Type I diabetes occurs when beta-cells of pancreas are destroyed and no more insulin is produced, and it often develops in childhood. Type II diabetes is induced when the amount of insulin secretion decreases or when the function of the insulin decreases due to the combination of multiple factors such as genes, obesity, lack of exercise, stress and aging. Ninety five percent of diabetes patients in Japan fall under this type.

### ■ Complications of diabetes

If you leave diabetes untreated, other diseases can be induced. These conditions are called complications. The complications distinctive to diabetes are “diabetic neuropathy,” “diabetic retinopathy,” and “diabetic nephropathy.”

“Diabetic neuropathy” occurs when nerves are denatured due to a persistently high level of blood sugar or when capillary vessels that deliver nutrition to the nerves develop problems and the blood circulation is disturbed. The patients with this complication may feel numbness or a sensation of worms crawling on their limbs. Sometimes, they do not feel any pain when they are injured or burned, so the wounds become infected and necrotized. This kind of serious complication can also happen. In addition, some people may also develop symptoms such as muscular atrophy or weakness, abdominal discomfort or dizziness.

“Diabetic retinopathy” occurs when many small blood vessels located behind the eyes that supply nutrition to the retina, are damaged due to the persistently high blood sugar level. Patients with this condition may lose their sight to some extent, and eventually become blind if the condition progresses. “Diabetic nephropathy” occurs when glomerular capillaries, which are responsible for filtering the blood in the kidneys, develop problems due to a persistently high blood sugar level. Patients with this condition have a decreased ability of filtering the blood. If it persists, they will no longer be able to filter the blood by themselves and will need to receive 3-5 hour dialysis twice or three times a week. This will affect their quality of life greatly.

### ■ Treatment of diabetes

You may think that you can just introduce insulin from outside the body to treat diabetes

because this disease occurs due to a lack of insulin. In 1921 insulin was first discovered, although diabetes itself had been known for a long time. With the help of Professor Macleod of the University of Toronto, a Canadian surgeon, Dr. Banting, successfully caused a decrease in the blood sugar level of dogs, in which the blood sugar had been raised by removing the pancreas, by using the extract of islets of Langerhans obtained from dog pancreas. In 1922, a substance extracted from bovine fetal pancreas was introduced to a 14 year old diabetic boy. With this treatment, he was able to recover from diabetic coma and live longer. This substance was named insulin after the Latin word for "islands." Banting and his colleagues received the Nobel Prize in Physiology or Medicine in 1923 for their achievement.

After this discovery, a Danish company Nordisk (currently called Novo Nordisk Pharma Ltd.) extracted insulin from bovines and used it for the treatment of diabetes. The time that insulin showed an effect at this time, however, was so short that they had to inject it many times a day. The company that resolved this problem was also Danish. They successfully developed long-acting insulin, which would make it possible for patients to have only one or two injections per day.

Even now, patients with Type I diabetes who do not secrete insulin, are treated with insulin from the beginning. On the other hand, patients with Type II diabetes first attempt to improve their blood sugar levels by controlling their diet or

taking physical exercise. If it does not go well, patients try to take various drugs. If it does not still control well, insulin is used to treat them.

### ■ Improvement of insulin

It is however dangerous to introduce proteins obtained from other animals to humans. Insulin had been used without any serious problems because the structure of animal insulin is similar to that of humans. Even so, it can still cause allergies or adverse reactions in humans. The best is to use human insulin in humans, but it is very difficult because human insulin can only be obtained from humans.

There are many diseases that occur due to the lack of a substance such as insulin, which people naturally develop. If we can produce a large quantity of such a substance, which is only available in small quantities, it will be a great advantage for the treatment of these diseases. Genetic recombination techniques actually made this come true. With this technique, we can make microorganisms produce insulin by connecting a human gene that plays a role in designing insulin production, to such microorganisms as E.coli or yeast. In this way, we no longer need to use animal insulin to treat diabetes.

### ■ Improvement of treatment tools

Patients need to inject insulin by themselves because they have to do it several times a day. Due to fear and the burden, many of them do not like using insulin. In order to reduce the pain, various tools have been invented. With

devices that are currently being used, such as the pen-type injector, patients hardly feel any pain and only have to adjust the dial to choose the amount of insulin that is injected.

drink may be developed in the future. It will be amazing if patients who need insulin can be treated without injections!



### ■ Future of insulin

Ever since insulin products were invented, pharmaceutical companies have been investigating treatment methods to supply insulin in a pattern that is closer to natural insulin secretion, and that is safer and easier to use for patients. New drugs have also been developed for Type II diabetes, so treatment with insulin is no longer the last resort. In other words, it is now possible to consider using insulin first to decrease the blood sugar level and to later switch the treatment to this new drug. Further efforts have also been made to produce better insulin products. Even an insulin