PREEMPTIVE MEDICINE—A CASE STUDY OF DIABETES—

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WHAT IS PREEMPTIVE MEDICINE?

Preemptive medicine is attracting interest as a new preventive strategy against diabetes and dementia. The preemptive medicine is a new concept in the medical fields. It uses personal data, including genetic data and other physiological information, as well as information about lifestyles, to predict the risk of illness and complications. The aim of this new concept is to delay or prevent the onset of diseases by using these predictions as the basis for preventive actions; in other words, preventive interventions. It can be said that a preemptive medicine is highly precise preventive measures utilizing data, and its approach is to make interventions after narrowing down individuals with a high risk of suffering a certain disease, based on scientific grounds. This approach has the potential to strengthen individual motivation toward efforts to delay or prevent the onset of disease, while at the same time reducing the cost of healthcare is expected. In this article, we will focus on notable trends relating to diabetes, a field in which preemptive medicine is expected to result in reductions of healthcare costs.

THE RISING NUMBER OF DIABETIC PATIENTS, AND THE HIGH COST OF TREATMENT

According to a report published in 2015 by the International Diabetes Federation (IDF), there are 415 million diabetic patients (aged 20-79) in the world. By 2040, this number is expected to climb to 642 million, which means that one in ten adults will be affected. Growth in the number of those afflicted with the disease is expected to be especially significant in the Western Pacific and Southeast Asia. Current estimates indicate that the number of diabetic patients in these regions will reach 214.8 million and 140.2 million, respectively. In 2015, the cost of diabetes treatment reached US$673 billion, or 12% of total world expenditure on healthcare. Because this rapid rise in the number of diabetic patients is likely to result in further increases in healthcare expenditure, measures to prevent or delay the onset of the disease will be an important social priority.

The severity of type 2 diabetes, which accounts for about 90% of total diabetes cases, can often be reduced if treatment is started before the symptoms appear, and this type is preventable through a healthy diet and

1 Diabetes Atlas http://www.diabetesatlas.org/
2 The Western Pacific Region (defined by the IDF) includes Japan, South Korea, North Korea, China, Mongolia, ASEAN countries, Australia, New Zealand, and Oceanian countries.
3 The South-East Asian Region (defined by the IDF) includes India, Bangladesh, Nepal, Bhutan, Sri Lanka, Maldives, and Malicious
4 Type 2 diabetes develops due to insulin deficiency caused by destruction of pancreatic β-cells. Most of the patients are children. Although it is being revealed that certain groups of people have a genetic predisposition to diabetes, the disease often develops after middle age due to obesity and lack of exercise.
moderate exercise. However, a survey by the Japan Diabetes Clinical Data Management Study Group shows that about 40% of type 2 diabetic patients also develop diabetic kidney disease (DKD), including mild symptoms. When conditions get aggravated, dialysis becomes necessary. Dialysis imposes a heavy burden on patients (standard treatment requires four-hour session, three times a week). Also, the cost is high, at around ¥5 million per year. From the viewpoint of reducing healthcare expenditure, expectations toward preemptive medicine for diabetes are rising. Without receiving medical checkups, if undiagnosed diabetics remain untreated for some time, they will be affected not only by DKD as mentioned above, but also by chronically high blood glucose levels, leading to complications such as diabetic retinopathy and diabetic neuropathy. That is why it is important to prevent or delay the onset of diabetes and its related complications.

**NOTABLE TRENDS RELATING TO PREEMPTIVE MEDICINE FOR DIABETES**

Preemptive medicine to delay or prevent the onset of diabetes and diabetes complications has four stages (see diagram).

**Diagram: The Stages of Diabetes and Preemptive Medicine (new concept of prevention)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>Stage 1</td>
<td>Educate and raise awareness toward preventing non-diabetic people from developing the disease</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Prevent the onset of diabetes in high-risk groups with a strong potential for developing the disease by using genetic testing and other methods</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Maintain appropriate blood glucose levels and prevent complications by giving lifestyle guidance and medication, as required, to people who are diagnosed with diabetes</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Prevent aggravation or complications in diabetic patients who are already being treated for the DKD</td>
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</tbody>
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Currently, a variety of intervention methods are being explored at each of these stages above. Some key trends are outlined below.
Stage 0 (pre-diabetes) preventive measures (① in the diagram):

The World Health Organization (WHO) is studying various diabetes preventive measures targeting healthy people, including public education activities, health surveys, and monitoring. Knowledge gained through this work will be made available globally and is likely to contribute to the development of preemptive medicine.

Early diagnosis through genetic testing (② in the diagram):

In the context of preemptive medicine, genetic testing is a research area that draws a lot of attention. Currently, however, in forecasting individuals’ diabetes risk, its accuracy still needs to be improved (To date, over 90 genes relating to diabetes have been identified). Type 2 diabetes results not only from genetics, but is caused by multiple factors, including environmental factors. Various research projects are in progress with the aim of predicting the risk of diabetes based on personal environmental factors, such as fetal environment, dietary habits in infancy, and exercise levels, in addition to genetic information. Also, because there are ethnic differences in the incidence of diabetes and complications, in Japan, under the guidance of the Japanese Ministry of Health, Labour and Welfare, the Japan Diabetes Society, the National Center for Global Health and Medicine, and other organizations are conducting a large-scale clinical program called the Japan Diabetes Outcome Intervention Trial (J-DOIT), which explores preventive methods suitable for Japanese. The goals of this program are to halve the diabetes onset ratio in people at high-risk, to halve the treatment interruption ratio, and to reduce the development of complications by 30%. Findings from this project are used to study measures to delay or prevent the onset of diabetes and diabetes complications for Japanese.

Development of blood glucose monitoring devices (③ in the diagram)

In the development of continuous blood glucose monitoring devices, one of the key priorities is the improvement of the patient’s QOL and to achieve that, the development of wearable devices that combine monitors with insulin delivery systems is underway. One such device is the MiniMed 620G system produced by Medtronic in Ireland.

A joint research team of the American venture company MC10, Inc. and Seoul National University in South Korea is developing a film-sheet like wearable device that is wrapped around about half of the wrist. While still at the basic research stage, this device will continuously monitor the blood glucose level in perspiration and, in response to level changes, automatically deliver the diabetes drug (Metformin) using a minimally invasive percutaneous mechanism. In the future, the development of a fully automatic drug delivery device, utilizing artificial intelligence and other technologies to forecast the changes of blood glucose levels, is expected.

Prevalence of diabetes monitoring apps (④ in the diagram)

In the United States, the FDA approved in 2010 the diabetes management app BlueStar (Welldoc, Inc.), which is designed both to motivate patients and get them to continue treatment and hospital attendance, and also to allow doctors to monitor home-care patients effectively. BlueStar is a patient intervention service that links to a blood glucose monitoring device. Before each examination, a report on the patient’s blood glucose levels, medication compliance, physical condition, and overall status is sent to the medical team, and this contributes to the efficiency of medical consultations. The study of type 2 diabetes patients (n = 163) indicated that the effectiveness of treatment was enhanced in patients using BlueStar (The blood glucose level; glycated hemoglobin [HbA1c] of BlueStar users reduced 1.2% compared with patients receiving only conventional treatment over a one-year period). Because the BlueStar app is based on scientific evidence, it is prescribed by doctors in the same way as conventional drugs and is eligible for reimbursements from several major US health insurance companies. The app also functions as an information sharing platform, and patients can learn about blood glucose management and the disease itself, and even ask specialists questions.
Sugar Clinics for low/medium-income earners (⑤ in the diagram)

In terms of physical platforms, there are sugar clinics. Clínicas del Azúcar is a healthcare center established by a graduate of Massachusetts Institute of Technology (MIT) Sloan School of Management, Javier Lozano in his home country Mexico in 2010, with the aim of preventing the aggravation of diabetes among low- and medium-income people. This is a new, one-stop shop type clinic, which encompasses a clinic, counseling center, testing facility, pharmacy, sales outlet for related products (such as low-sugar foods and foot care products and shoes for patients with gangrenous feet), and a community center (with exercise classes, nutrition education). There are now nine of these facilities. By paying about US$300 per year, members are able to access all of the services, and buy drugs offered at discounted prices by using the centralized purchasing system.

KEY REQUIREMENTS FOR THE IMPLEMENTATION OF PREEMPTIVE MEDICINE

Going forward, we can expect to see continuing research efforts targeting the effective implementation of preemptive medicine in the field of diabetes, such as the advancing technologies for diagnostics, and various interventions related to risk-based approach. One priority in this context will be the expanding data sharing, with protections of personal data such as genetic information. Large-scale data analyses combining physiological and environmental factors are expected to lead to a better understanding of the types of people who have a high risk of being affected by diabetes, and which preemptive medicine will be effective, and thereby the establishment of more personalized preventive strategies are expected. In order for these diagnostic technologies and intervention services to fully function in the society, there are high hopes for growth in patient intervention services linked with medical services, such as diabetes management apps, and sugar clinics, as service access platforms.

To ensure the prevalence of these services and products, they will need to be rolled out in ways that align with the state of healthcare systems in each country. When sugar clinics become more common, combining these clinics with apps will contribute to the achievement of greater efficiency in patient care, and the introduction of preemptive medicine.