

A review on Diabetes, Biosensors and Continuous Glucose Monitoring

^{1*}Ritwija Bhattacharjee, ²Dr. Pushpa Agrawal and ³Dr. Neeta Shivakumar

¹²³Department of Biotechnology, RV College of Engineering, Bangalore-560 059, Karnataka, India

Abstract: Diabetes is a group of diseases that cause blood sugar levels to become too high. It is one most common disease, that can influence other disease. It is important to bring it under control. Monitoring glucose during the past two decades has developed techniques and approaches. In the literature, electrochemical measurements are reported in greater quantities than other methods. This makes them the main subject of this analysis. As a result of their high selectivity for glucose measurement, biosensors remain a main focus of most teams. The principles and types of glucose monitoring sensors are presented in a systematized and classified fashion.. Various design approaches for glucose biosensors are discussed, including needle-type sensors, sensors intended for chronic implantation, and the combination of glucose biosensors with micro dialysis sampling. Continuous glucose monitoring can help to treat better and immediately whenever need.

Keywords: diabetes, monitoring, biosensors, continuous glucose monitoring

INTRODUCTION

An individual with diabetes experiences elevated blood glucose levels and abnormal fats and protein metabolism as part of their disease. A child, teenager, or young adult is more likely to be diagnosed with Type 1 diabetes. It is unknown what caused the incident. It is believed that the cause of type 1 diabetes is a combination of genetic susceptibility and environmental factors. The cause of a significant proportion of cases concerning the biological, chemical, nutritional, and behavioural components hasn't as yet been proven beyond a reasonable doubt despite extensive research into these components. Diabetes type 2 can be prevented by better understanding the risk factors associated with the disease. The genetic component, however, plays a small but important role, whilst other risk factors like age, overweight, and inactivity decrease chances of developing the disease. Besides smoking, obesity is the greatest risk factor for diabetes. However, smoking has also been shown to increase the risk of diabetes. Excess fat in the body can cause diabetes in some ethnic groups, such as Southeast Asians. The consumption of foods with high sugar and fat content has also been linked to an increased risk of type 2 diabetes. Uncontrolled diabetes can lead to complications in many organs due to the same risk factors as for type 2 diabetes. Amputation of lower limbs occurs when small blood vessels or large blood vessels are damaged. On the other hand, injuries to the brain and spinal cord cause loss of vision and kidney function. Type 2 diabetes, which accounts for the majority of diabetes cases, causes disability and shortens lives. It is preventable to a great extent due to its age, overweight, obesity, inactivity and excess weight gain during pregnancy. Diabetes type 1 is a chronic disease with no definitive cause, and it remains unpreventable. We have tried a number of strategies, but none have proved to be successful. Continuous glucose monitoring provides information about blood glucose fluctuations such as their direction, magnitude, duration, frequency, and causes. With continuous monitoring, glucose levels can be assessed throughout the day in much greater detail than with conventional intensified glucose monitoring, defined as measuring three to four times per day. Monitoring glucose levels continuously can provide valuable information about trends in glucose levels, which can help to identify and prevent unwanted periods of hypo- or hyperglycaemia. [1][2][3][4][5][6]

Glucose

The word glucose is also used to refer to blood sugar. It is crucial for the body's mechanisms to be well-powered with glucose. Oftentimes, diabetes goes unnoticed when glucose levels are optimal. Our bodies revert to their healthy functions, when they stray from recommended boundaries. A monosaccharide, it is the simplest of the carbohydrates. It contains one sugar. It's not the only one. Among other monosaccharides, galactose, ribose, and fructose are also present. As one of the body's main sources of energy, glucose also comes from carbohydrates. Bread, fruit, and vegetables are all great sources of glucose. Food helps you stay alive by supplying the energy you need. Like many things, glucose should be consumed in moderation. An unhealthy or uncontrolled glucose level can have long-term and serious effects. What is the body's process for metabolizing glucose? Ideally, our bodies process glucose several times per day. We begin processing glucose immediately after eating. As enzymes help break down food, the pancreas, which produces hormones including insulin, interacts with how our body deals with glucose. After eating, our bodies signal to the pancreas that it needs to release insulin to deal with rising blood sugar levels. Nevertheless, some people can't depend on their pancreas

to step in and do the job they need. If the pancreas is unable to produce insulin, diabetes occurs. As a result, people with diabetes require outside assistance (insulin injections) to process and control glucose in their bodies. There is also insulin resistance in diabetes, wherein the liver fails to recognize insulin in the body and makes excessive amounts of glucose. As glucose is stored in the liver and is converted into glucose when it is needed, the liver plays an important role in sugar control. An insufficient level of insulin in the body can cause free fatty acids to be released from fat stores. A condition called ketoacidosis results from this. The liver produces ketone bodies as waste products when it breaks down fat. In large quantities, ketone bodies can be toxic. [7][8][9][10][11][12]

0-3 hours

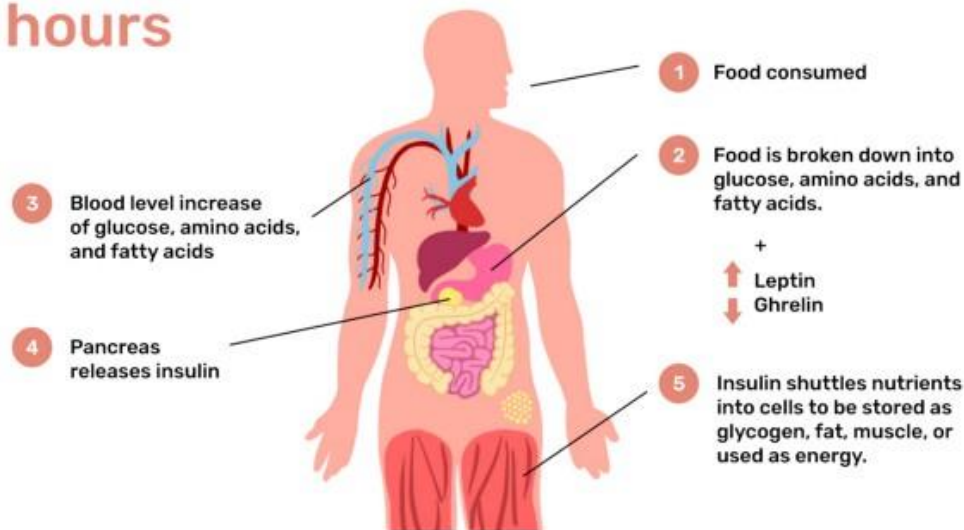


Figure 1: cycle of food to energy.

Diabetes

Diabetes occurs when the body is incapable of taking in sugar (glucose) and using it for energy. An uncontrolled diabetes condition can damage the heart, kidneys, eyes, and nerves, as well as other organs and tissues in the body. Our bodies break down food into a range of nutrients by way of digestion. Whenever we consume carbohydrates (like bread, rice, pasta), the body converts them into sugar (glucose). When glucose is in bloodstream, it must be helped - a "key" - in order to reach its final destination, which is inside the body's cells (the cells make up organs and tissues). Insulin is the "key" "An organ above the stomach called the pancreas, which makes insulin, delivers it into the bloodstream. A cell's "door" is opened by insulin, allowing glucose to enter the body's cells. An organ or tissue needs glucose for proper functioning as it provides energy to the body. We are diabetic if: 1. There is not enough insulin produced by the pancreas. 2. Insulin is made by the pancreas, but the cells of the body do not react to it and are not able to utilize it normally. Blood glucose levels rise if glucose cannot enter cells in the body.[14][15]

Types

1. Type 1 diabetes- It is an autoimmune disease, which means our bodies attack themselves. This leads to the destruction of insulin-producing cells in the pancreas. Diabetes type 1 affects up to ten percent of diabetics. Children and young adults are most commonly affected (although it can occur at any age). Previously, it was called "juvenile" diabetes. Diabetes type 1 requires daily insulin injections. Because of this, it is also called insulin-dependent diabetes.
2. Type 2 diabetes- A person with type 2 diabetes will either not produce enough insulin or their cells will not respond properly to insulin. The most common form of diabetes. 95% of those with diabetes have the type 2 form. People in their middle and old age are usually affected. Among the other common names for Type 2 diabetes, there are adult-onset diabetes and insulin-resistant diabetes. The term "a touch of sugar" may have come from our parents or grandparents.
3. Prediabetes- This type of diabetes occurs before type 2 diabetes, referring to blood glucose levels that are higher than normal but not sufficiently high to be diagnosed as type 2 diabetes
4. Gestational- Some women develop gestational diabetes while pregnant. Gestational diabetes usually, whereas gestational diabetes usually disappears after delivery. However, chronic gestational diabetes puts us at higher risk for developing type 2 diabetes in the future. [16][17][18][19][20]

Approximately 463 million people are living with diabetes throughout the world and 88 million are in Southeast Asia, according to data from the International Diabetes Federation (IDF). Approximately 463 million people are living with diabetes throughout the world and 88 million are in Southeast Asia, according to data from the International Diabetes Federation (IDF). 77 million of these 88 million people are Indian. According to the IDF, diabetes is prevalent in 8.9%

of the population. According to estimates from the IDF, India has the second highest rate of children with type 1 diabetes, behind the United States. A significant number of type 1 diabetic children in the SEA region also suffer from this condition. The country is considered to have 77 million people with diabetes, making it the second worst affected country in the world, behind China. One in six people with diabetes worldwide (17%) is Indian. As reported by World Health Organization, 2 percent of Indian deaths are caused by diabetes. (India's population is approximately 17.5% of the world's total.) According to the International Diabetes Federation, there will be 134 million with diabetes by 2045. [21][22][23][24][25]

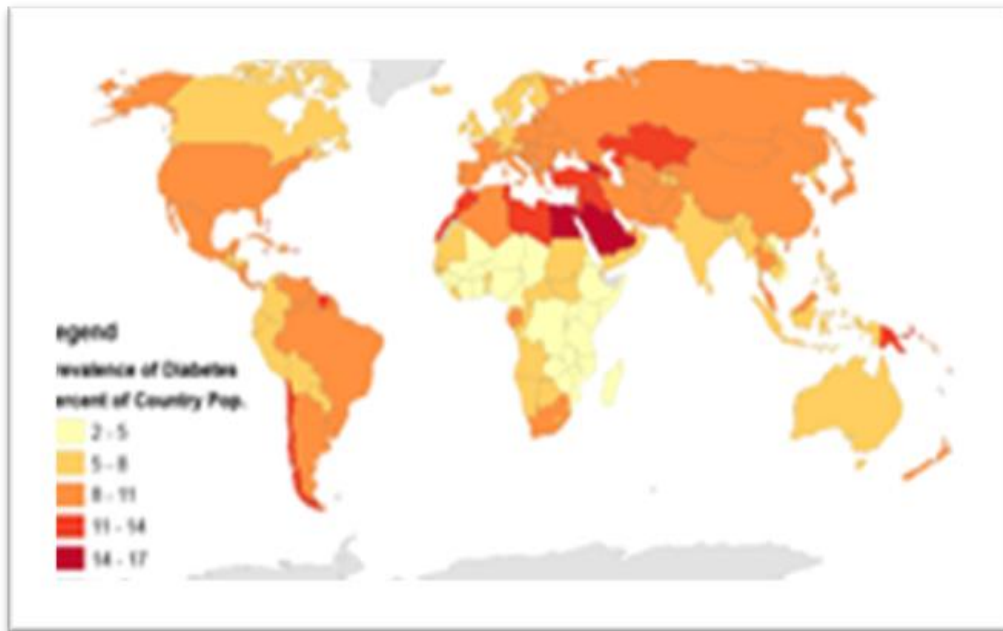


Figure 2: The diabetes rate in 2014. Globally, 9.2% of people had the condition. According to the 2020 census, it is 8.9%.

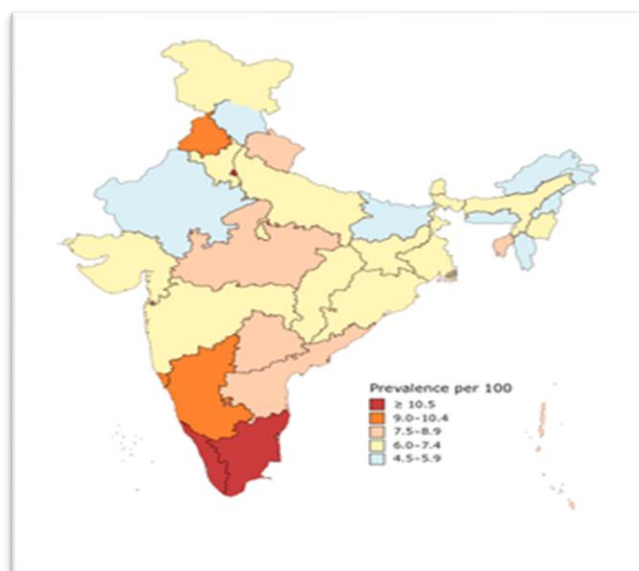


Figure 3: Figures of diabetes rates in 2016 in Indian states

The risk factors: Diabetes develops differently for each of us depending on the factors that increase our risk. Risk factors for type 1 diabetes include: Having a family history, Injury to the pancreas, Presence of autoantibodies, Physical stress, Exposure to illnesses caused by viruses. Risk factors for prediabetes and type 2 diabetes include: Family history (parent or sibling) of prediabetes or type 2 diabetes, Being African-American, Hispanic, Native American, Asian-American race

or Pacific Islander, Being overweight, Having pressure, Having low HDL cholesterol and high triglyceride level, Being physically inactive, Being age 45 or older, Having gestational diabetes or giving birth to a baby weighing more than 9 pounds. Having syndrome, Having a history of heart disease or stroke, Being a smoker, Risk factors for gestational diabetes include, Family history (parent or sibling) of prediabetes or type 2 diabetes, Being African-American, Hispanic, Native American or Asian-American, Being overweight before your pregnancy, Being over 25 years of age. Symptoms of diabetes: 1) Increased thirst. 2) Weak, tired feeling. 3) Blurred vision. 4) Numbness or tingling in the hands or feet. 5) Slow-healing sores or cuts. 6) Unplanned weight loss. 7) Frequent urination. 8) Frequent unexplained infections. 9) Dry mouth. Other symptoms, In women: Dry and itchy skin, and frequent yeast infections or urinary tract infections., In men: Decreased sex drive, erectile dysfunction, decreased muscle strength. Type 1 diabetes symptoms: Symptoms can develop quickly – over a few weeks or months. Symptoms begin when we’re young – as a child, teen or young adult. Additional symptoms include nausea, vomiting or stomach pains and yeast infections or urinary tract infections. Type 2 diabetes and prediabetes symptoms: We may not have any symptoms at all or may not notice them since they develop slowly over several years. Symptoms usually begin to develop when we’re an adult, but prediabetes and type 2 diabetes is on the rise in all age groups. Gestational diabetes: we typically will not notice symptoms. our obstetrician will test you for gestational diabetes between 24 and 28 weeks of our pregnancy. Complications of diabetes: If our blood glucose level remains high over a long period of time, our body’s tissues and organs can be seriously damaged. Some complications can be life-threatening over time: Cardiovascular issues including coronary artery disease, chest pain, heart attack, stroke, high blood pressure, high cholesterol, atherosclerosis (narrowing of the arteries), Nerve damage (neuropathy) that causes numbing and tingling that starts at toes or fingers then spreads, Kidney damage (nephropathy) that can lead to kidney failure or the need for dialysis or transplant, Eye damage (retinopathy) that can lead to blindness; cataracts, glaucoma, Foot damage including nerve damage, poor blood flow and poor healing of cuts and sores, Skin infections, Erectile dysfunction, loss., Depression, Dementia, Dental problems, Complications of gestational diabetes: In the mother: Preeclampsia (high blood pressure, excess protein in urine, leg/feet swelling), risk of gestational diabetes during future pregnancies and risk of diabetes later in life, In the new born: Higher-than-normal birth weight, low blood sugar (hypoglycaemia), higher risk of developing type 2 diabetes over time and death shortly after birth. [26][27][28][29][30][31][32][33][34][35][36]

Diagnosis:

Diabetes is diagnosed and managed by checking your glucose level in a blood test. There are three tests that can measure your blood glucose level: fasting glucose test, random glucose test and A1c test. Fasting plasma glucose test: This test is best done in the morning after an eight hour fast (nothing to eat or drink except sips of water). Random plasma glucose test: This test can be done any time without the need to fast. A1c test: This test, also called HbA1C or glycated haemoglobin test, provides your average blood glucose level over the past two to three months. This test measures the amount of glucose attached to haemoglobin, the protein in your red blood cells that carries oxygen. You don’t need to fast before this test. Oral glucose tolerance test: In this test, blood glucose level is first measured after an overnight fast. Then you drink a sugary drink. Your blood glucose level is then checked at hours one, two and three. Gestational diabetes tests: There are two blood glucose tests if you are pregnant. With a glucose challenge test, you drink a sugary liquid and your glucose level is checked one hour later. You don’t need to fast before this test. If this test shows a higher-than-normal level of glucose (over 140 mg/dL), an oral glucose tolerance test will follow (as described above). Type 1 diabetes: If your healthcare provider suspects type 1 diabetes, blood and urine samples will be collected and tested. The blood is checked for autoantibodies (an autoimmune sign that your body is attacking itself). The urine is checked for the presence of ketones (a sign your body is burning fat as its energy supply). These signs indicate type 1 diabetes. [37][38][39][40][41]

Type of test	Normal (mg/dL)	Prediabetes (mg/dL)	Diabetes (mg/dL)
Fasting glucose test	Less than 100	100-125	126 or higher
Random (anytime) glucose test	Less than 140	140-199	200 or higher
A1c test	Less than 5.7%	5.7 - 6.4%	6.5% or higher
Oral glucose tolerance test	Less than 140	140-199	200 or higher

Figure 4: Range for blood sugar

Blood Glucose Monitoring

Blood Glucose Monitoring is a way of checking the concentration of glucose in the blood using a glucometer. Provides quick response to tell if the sugar is high or low indicating a change in diet, exercise or insulin. Over time, it reveals individual of blood glucose changes. Reduces risk of developing complications with diabetes. Allows diabetics to see if the insulin and other medications they are taking are working. Gives diabetics an idea as to how exercise and food affect their blood sugar. May prevent hypoglycaemia or hyperglycaemia. Types of glucose biosensors Enzymatic glucose biosensors: First generation glucose biosensor, second generation glucose biosensor, third generation glucose biosensor non-enzymatic glucose biosensors. 1st generation: the normal product of the reaction diffuses to the transducer and causes electrical response. 2nd generation: involves specific mediators between reaction and transducer to generate improved response. 3rd generation: reaction itself causes the response First generation glucose biosensors. The first-generation glucose biosensors estimated glucose concentration in the sample based on hydrogen peroxide production by glucose oxidase utilizing dissolved oxygen. Based on this technology, yellow spring Instrument company, launched the first commercial glucose biosensor in market in 1975 for the direct measurement of glucose. The usage of the most expensive metal platinum for the fabrication of this electrode restricted the biosensor to clinical laboratories only. Major drawbacks of first-generation glucose biosensors. Amperometric measurement of hydrogen peroxide required a high operating potential (0.6 V) for high selectivity. Restricted solubility of oxygen in biological fluids, which produced fluctuations in the oxygen tension. Deactivation of the enzyme due to the production of hydrogen peroxide. Second generation glucose biosensor the second-generation glucose biosensor utilized redox mediator to transfer electrons from the enzyme to the working electrode surface. A variety of redox mediators, such as ferrocene, ferricyanide, quinines, methylene blue etc were used to improve sensor performance. Usage of redox mediator eliminated the need of oxygen for electron transfer at the electrode surface, thus overcoming the drawback of limited oxygen pressure observed in the first-generation biosensor. The lower redox potential of chosen mediators (0-2 V) results in no interference from other electroactive species such as uric acid, ascorbic acid. Redox mediator enhances the electron transfer between the redox centre of enzyme and the electrode surface. Major drawbacks of second-generation glucose biosensors. High competition between redox mediator and oxygen. Interference of other electroactive species lead to false and inaccurate results. Small size and highly diffusive nature of mediators poses problem of leaching of mediator from intermediate region between enzyme and electrode surface. Third generation glucose biosensors the third-generation glucose biosensors are based on the direct electron transfer between the active centre of enzyme and the electrode. The intrinsic barrier to electron flow is the globular structure of glucose oxidase with the active site, containing FAD/FADH₂ redox cofactor, buried deep inside a cavity of ~ 13 Å is a major hinderance for direct electron transfer. Carbon nanotubes immobilized electrode surface provide suitable orientation for enzyme immobilization and establish connection between electrode surface and deeply. Non-enzymatic[41][42][43]

Glucose biosensors

The use of non-enzymatic electrodes as glucose sensors potentially promises a fourth generation to analytical glucose oxidation. The active metal nanoparticle undergoes an oxidation step that forms a hydrous oxide layer OH ads that mediate oxidation of the adsorbed species. Glucose Biosensors Based on Carbon Nanotube Nano electrode Ensembles. The development of glucose biosensors based on carbon nanotube (CNT) Nano electrode ensembles (NEEs) for the selective detection of glucose. CNTs have a high electrocatalytic effect and a fast electron-transfer rate. Glucose oxidase was covalently immobilized on CNT NEEs via carbodiimide chemistry by forming amide linkages between their amine residues and carboxylic acid groups on the CNT tips. The catalytic reduction of hydrogen peroxide liberated from the enzymatic reaction of glucose oxidase upon the glucose and oxygen on CNT NEEs leads to the selective detection of glucose. The biosensor effectively performs a selective electrochemical analysis of glucose in the presence of common interferents (e.g., acetaminophen, uric and ascorbic acids), avoiding the generation of an overlapping signal from such interferents. Such an operation eliminates the need for permselective membrane barriers or artificial electron mediators, thus greatly simplifying the sensor design and fabrication. The fabrication of glucose biosensors based on CNT NEEs for the selective and sensitive detection of glucose. CNT NEEs eliminate potential interference through the preferential detection of hydrogen peroxide. Such development of interference-free transducers should simplify the design and fabrication of conventional and miniaturized sensing probes. The glucose biosensor based on an aligned CNT NEE is thus suitable for the highly selective detection of glucose in a variety of biological fluids (e.g., saliva, sweat, urine, and serum). The biosensor fabrication technology demonstrated in this work is readily applicable to the fabrication of other biosensors based on oxidases, such as biosensors for cholesterol, alcohol, lactate, acetylcholine, choline, hypoxanthine, and xanthine. Glucose biosensor test strips: Reduced mediators are formed and reoxidized at the electrode, providing an electrical signal to be measured. A blood glucose test is typically performed by pricking the finger to draw blood, which is then applied to a disposable "test-strip". ... Blood Glucose Sensor. (a) Example of a Commercial Product.[44][45][46]

Continuous glucose monitoring

Continuous glucose monitoring automatically tracks blood glucose levels, also called blood sugar, throughout the day and night. It sees glucose level anytime at a glance. Also review how your glucose changes over a few hours or days to see trends. Seeing glucose levels in real time can help you make more informed decisions throughout the day about how to balance your food, physical activity, and medicines. A CGM works through a tiny sensor inserted under skin, usually on belly or arm. The sensor measures your interstitial glucose level, which is the glucose found in the fluid between the cells. The sensor tests glucose every few minutes. A transmitter wirelessly sends the information to a monitor. The monitor may be part of an insulin pump or a separate device, which you might carry in a pocket or purse. Some CGMs send information directly to a smartphone or tablet. Special Features of a CGM, CGMs are always on and recording glucose levels—whether showering, working, exercising, or sleeping. Many CGMs have special features that work with information from glucose readings: An alarm can sound when glucose level goes too low or too high. Some models can send information right away to a second person's smartphone—perhaps a parent, partner, or caregiver. For example, if a child's glucose drops dangerously low overnight, the CGM could be set to wake a parent in the next room. Currently, one CGM model is approved for treatment decisions, the Dexcom G5 Mobile. That means it can make changes to diabetes care plan based on CGM results alone. With other models, one must first confirm a CGM reading with a finger-stick blood glucose test before you take insulin or treat hypoglycemia. Special Requirements Needed to Use a CGM: Twice a day, check the CGM itself. a drop of blood is tested on a standard glucose meter. The glucose reading should be similar on both devices, also need to replace the CGM sensor every 3 to 7 days, depending on the model. For safety it's important to take action when a CGM alarm sounds about high or low blood glucose. Most people who use CGMs have type 1 diabetes. Research is underway to learn how CGMs might help people with type 2 diabetes. CGMs are approved for use by adults and children with a doctor's prescription. Some models may be used for children as young as age 2, doctor may recommend a CGM children: are on intensive insulin therapy, also called tight blood sugar control have hypoglycemia unawareness often have high or low blood glucose, doctor may suggest using a CGM system all the time or only for a few days to help adjust diabetes care plan. Benefits of a CGM: Compared with a standard blood glucose meter, using a CGM system can help in better manage glucose levels every day, have fewer low blood glucose emergencies, need fewer finger sticks. A graphic on the CGM screen shows whether glucose is rising or dropping—and how quickly—so one can choose the best way to reach your target glucose level. Over time, good management of glucose greatly helps people with diabetes stay healthy and prevent complications of the disease. People who gain the largest benefit from a CGM are those who use it every day or nearly every day.[47][48]

What is the process of taking insulin?

There are various ways for you to obtain insulin; your healthcare provider will determine which is right for you based on your preferences, lifestyle and insulin needs. A needle and syringe are inserted into a vial of insulin, a syringe is pulled back, and the needle is filled with one or more doses of insulin. One or more shots of insulin are required each day to maintain your target blood sugar level. Injections are done in your belly, thigh, buttocks or upper arm - rotating injection spots. A pen-like device that comes with an insulin cap is the insulin pen. Insulin pumps are small, computerized devices used to administer insulin; they are worn on your belt, pocket, or underneath clothing. Through a flexible tube called a cannula they deliver insulin 24 hours a day. Under the skin, a needle is used to insert the cannula. When the cannula is replaced every two to three days, the needle is removed and just the flexible tube is left under the skin. Another type of insulin pump attaches directly to the skin. Using an insulin pump in conjunction with a continuous glucose monitor is an artificial pancreas (also called a closed loop insulin delivery system). In response, the pump delivers insulin as needed based on measuring blood glucose levels every five minutes. With insulin inhalers you introduce powdered inhaler into your lungs through a mouthpiece where you inhale it in. Inhaled insulin is absorbed by the lungs, then enters the bloodstream. Diabetes type 1 and type 2 patients can only use inhalers. Ports for the injection of insulin: These are small tubes placed under the skin to deliver insulin. You can inject insulin through this port with a needle and syringe or insulin pen by using an adhesive patch to keep the port in place. Changing the port happens every few days. A port is convenient because it eliminates rotating injection sites. The jet injector delivers insulin through the skin via a fine spray using high pressure to avoid needles.[49][50][51]

Artificial pancreas: The artificial pancreas system, which people with diabetes have begun incorporating into their daily lives, includes CGMs. In developing artificial pancreas technology, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has played a pivotal role. In order to reduce blood glucose levels, artificial pancreas should be used instead of blood glucose testing and insulin shots. With a system that monitors blood glucose levels constantly, insulin or both insulin and glucagon are automatically administered. In addition to remote monitoring, parents and medical personnel can also access the system. The United States reported its 2016 economic data in January. An artificial pancreas system with closed-loop technology is approved by the Food and Drug Administration. You are tested for glucose every 5 minutes during the day and night through an implanted CGM, and insulin is automatically given in just the right amount through a separate insulin pump. A glucose meter should still be used to monitor your blood sugar levels, and the pump should be adjusted to deliver an appropriate amount of insulin at mealtimes and whenever you need

corrections. You can sleep through the night using this closed-loop system instead of managing your blood sugar daily, can sleep through the night without checking glucose levels or taking any medication.[52][53]

Insulin pump: Infusion pumps (or insulin pumps for short) deliver insulin to the body by continuous subcutaneous infusion (CSII). CSII pumps are pager-sized devices that can be connected to the body through an infusion set. Disposable insulin reservoirs and disposable infusion sets with cannulas for subcutaneous insertion and tubing systems connect insulin reservoirs to cannulas are the components of the kit. Diabetes mellitus cannot be managed with insulin pump therapy alone. Insulin pens and syringes are regarded as inferior delivery mechanisms for administering insulin. A properly programmed insulin pump should deliver insulin through the subcutaneous vein near the same speed as a healthy pancreas would. Other methods of delivering insulin do not do this. An absolute prerequisite for going on a pump is patient willingness. Pump therapy does not become an option merely because a patient wishes to receive it. In addition to those listed below, a patient must also have the following conditions to be considered for pump therapy. The patient should not be placed on the pump if, despite the explanation and counseling, he or she does not feel comfortable wearing it despite meeting the requirements. Patients who frequently experience severe hypoglycemia Basal infusions are delivered at tiny rates by the insulin pump, 0.1 to 2 U/h. Low blood glucose levels are extremely unlikely to result from such small amounts of insulin. A second benefit is that regular insulin and rapid-acting insulin analogs employed in the pump both have a short half-life and are rapidly degraded, therefore minimising the risk of insulin accumulation and hypoglycemia. The new generation of "smart" insulin pumps come with features that patients and caregivers can use to schedule the insulin sensitivity factor and also use the Bolus Wizard feature to calculate and administer insulin based on the carbohydrate content in the diet and blood glucose values. Physiological insulin secretion is achieved through the use of these functions under certain circumstances mimicking a normal pancreatic function. In this case, there's no reason why extra insulin would be delivered when using an insulin pump. With the Bolus Wizard, insulin can also be administered according to the phenomenon of bolus on board, which occurs when a previously administered bolus is available in the bloodstream. Furthermore, excessive low sugar episodes will be prevented. Through the studies in which CSII has been evaluated, either minimal hypoglycemia has occurred or none at all.[54][55]

CONCLUSION

If you do not understand a patient's glycemic pattern, continuous glucose monitoring is an advantage over intermittent glucose monitoring. When glucose levels of blood are monitored intermittently, one cannot obtain the same level of information obtained by continuous glucose monitoring regarding direction, magnitude, duration, frequency, and causes of fluctuations in blood sugar levels. CGM can allow retrospective patterns to be captured and used for adjusting therapy or identifying physiology parameters. In cases when it is important to recognize both trend patterns as well as absolute magnitudes of glycemia in real time, a real-time CGM is an invaluable tool. The patient must be educated on how to use continuous glucose monitoring technology. CGMs may provide inaccurate readings during hypoglycemia or rapid fluctuations. Continuous glucose monitoring appears to improve either mean glycemia or hypoglycemia burden, according to clinical outcomes studies, but more evidence is needed to persuade payers to cover this technology. As a global economy constantly hungry for data, it appears likely that CGMs will eventually become an integral part of diabetes management, initially for diabetics who have difficulty controlling the condition, and then eventually for most diabetic patients. In time, retrospective reporting will give way to real-time readings, and adjunctive use, which requires confirmation by means of a finger-stick blood test, will be replaced with primary use that does not require any confirmation. In the near future, diabetic patients will have more access to continuous monitoring methods that require minimally invasive or noninvasive procedures. As diabetes management advances in the 21st century, CGMs will increasingly provide a roadmap for controlling the disease.

REFERENCE

1. Gross TM, Bode BW, Einhorn D, Kayne DM, Reed JH, White NH, Mastrototaro JJ: Performance evaluation of the MiniMed continuous glucose monitoring system during patient home use. *Diabetes Technol Ther* **2**: 49–56, 2000
2. Potts RO, Tamada JA, Tierney MJ: Glucose monitoring by reverse iontophoresis. *Diabetes Metab Res Rev* **18 (Suppl. 1)**:S49–S53, 2002
3. Bode B, Gross K, Rikalo N, Schwartz S, Wahl T, Page C, Gross T, Mastrototaro J: Alarms based on real-time sensor glucose values alert patients to hypo- and hyperglycemia: the guardian continuous monitoring system. *Diabetes Technol Ther* **6**:105–113, 2004
4. Maran A, Crepaldi C, Tiengo A, Grassi G, Vitali E, Pagano G, Bistoni S, Calabrese G, Santeusano F, Leonetti F, Ribaldo M, Di Mario U, Annuzzi G, Genovese S, Riccardi G, Previti M, Cucinotta D, Giorgino F, Bellomo A, Giorgino R, Poscia A, Varalli M: Continuous subcutaneous glucose monitoring in diabetic patients: a multicenter analysis. *Diabetes Care* **25**:347–352, 2002
5. Pfuetzner A, Caduff A, Larbig M, Schrepfer T, Forst T: Impact of posture and fixation technique on impedance spectroscopy used for continuous and non-invasive glucose monitoring. *Diabetes Technol Ther* **6**:435–441, 2004
6. Roglic, Gojka. "WHO Global report on diabetes: A summary." *International Journal of Noncommunicable Diseases* 1.1 (2016): 3.
7. Boerio-Goates, Juliana (1991), "Heat-capacity measurements and thermodynamic functions of crystalline α -D-glucose at temperatures from 10K to 340K", *J. Chem. Thermodynam.*, **23** (5): 403–09, doi:10.1016/S0021-9614(05)80128-4



8. Ponomarev, V. V.; Migarskaya, L. B. (1960), "Heats of combustion of some amino-acids", *Russ. J. Phys. Chem. (Engl. Transl.)*, **34**: 1182–83
9. Domb, Abraham J.; Kost, Joseph; Wiseman, David (1998-02-04). *Handbook of Biodegradable Polymers*. p. 275. ISBN 978-1-4200-4936-7.
10. Kamide, Kenji (2005). *Cellulose and Cellulose Derivatives: Molecular Characterization and its Applications* (1st ed.). Amsterdam: Elsevier. p. 1. ISBN 9780080454443. Retrieved 13 May 2021.
11. Jump up to:^{a b} World Health Organization (2019). World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization. hdl:10665/325771. WHO/MVP/EMP/IAU/2019.06. License: CC BY-NC-SA 3.0 IGO.
12. "Online Etymology Dictionary". *Etymonline.com*. Archived from the original on 2016-11-26. Retrieved 2016-11-25.
13. "Diabetes Blue Circle Symbol". International Diabetes Federation. 17 March 2006. Archived from the original on 5 August 2007.
14. Jump up to:^{a b c d e f g h i j k l m n o p q r s t u v w x} "Diabetes Fact sheet N°312". WHO. October 2013. Archived from the original on 26 August 2013. Retrieved 25 March 2014.
15. Jump up to:^{a b} Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN (July 2009). "Hyperglycemic crises in adult patients with diabetes". *Diabetes Care*. **32** (7): 1335–43. doi:10.2337/dc09-9032. PMC 2699725. PMID 19564476.
16. Krishnasamy S, Abell TL (July 2018). "Diabetic Gastroparesis: Principles and Current Trends in Management". *Diabetes Therapy*. **9** (Suppl 1): 1–42. doi:10.1007/s13300-018-0454-9. PMC 6028327. PMID 29934758.
17. Jump up to:^{a b} Saedi, E; Gheini, MR; Faiz, F; Arami, MA (15 September 2016). "Diabetes mellitus and cognitive impairments". *World Journal of Diabetes*. **7** (17): 412–22. doi:10.4239/wjd.v7.i17.412. PMC 5027005. PMID 27660698.
18. Jump up to:^{a b} Chiang JL, Kirkman MS, Laffel LM, Peters AL (July 2014). "Type 1 diabetes through the life span: a position statement of the American Diabetes Association". *Diabetes Care*. **37**(7): 2034–54. doi:10.2337/dc14-1140. PMC 5865481. PMID 24935775.
19. "Causes of Diabetes". National Institute of Diabetes and Digestive and Kidney Diseases. June 2014. Archived from the original on 2 February 2016. Retrieved 10 February 2016.
20. Jump up to:^{a b c d} Ripsin, CM; Kang, H; Urban, RJ (January 2009). "Management of blood glucose in type 2 diabetes mellitus" (PDF). *American Family Physician*. **79** (1): 29–36. PMID 19145963. Archived (PDF) from the original on 2013-05-05.
21. Divers J, Mayer-Davis EJ, Lawrence JM, et al. Trends in Incidence of Type 1 and Type 2 Diabetes Among Youths— Selected Counties and Indian Reservations, United States, 2002–2015. *MMWR Morb Mortal Wkly Rep*. 2020 Feb 14;69(6):161–165.
22. Su X, Kong Y, Peng D. Evidence for changing lipid management strategy to focus on non-high density lipoprotein cholesterol. *Lipids Health Dis*. 2019 Jun 7;18(1):134.
23. American Diabetes Association. Standards of Medical Care in Diabetes—2019. *Diabetes Care*. 2019 Jan 1; 42 (Supplement 1).
24. Centers for Disease Control and Prevention. National Center for Health Statistics. Underlying Cause of Death 1999–2017 on CDC WONDER Online Database, 2018. Accessed at <http://wonder.cdc.gov/ucd-icd10.html> on Oct 10, 2019.
25. American Diabetes Association. Economic costs of diabetes in the US in 2017. *Diabetes Care*. 2018 May;41(5):917–928.
26. "Classification of Diabetes mellitus 2019". WHO. Retrieved 2020-11-09.
27. Tuomi T, Santoro N, Caprio S, Cai M, Weng J, Groop L (March 2014). "The many faces of diabetes: a disease with increasing heterogeneity". *Lancet*. **383** (9922): 1084–94. doi:10.1016/S0140-6736(13)62219-9. PMID 24315621. S2CID 12679248.
28. "Definition of Diabetes mellitus". *MedicineNet*. Retrieved 2019-11-04.
29. Rother KI (April 2007). "Diabetes treatment—bridging the divide". *The New England Journal of Medicine*. **356** (15): 1499–501. doi:10.1056/NEJMp078030. PMC 4152979. PMID 17429082.
30. Jump up to:^{a b} "Diabetes Mellitus (DM): Diabetes Mellitus and Disorders of Carbohydrate Metabolism: Merck Manual Professional". Merck Publishing. April 2010. Archived from the original on 2010-07-28. Retrieved 2010-07-30.
31. Dörner M, Pinget M, Brogard JM (May 1977). "[Essential labile diabetes (author's transl)]". *MMW, Munchener Medizinische Wochenschrift* (in German). **119** (19): 671–74. PMID 406527.
32. Jump up to:^{a b} Petzold A, Solimena M, Knoch KP (October 2015). "Mechanisms of Beta Cell Dysfunction Associated With Viral Infection". *Current Diabetes Reports* (Review). **15** (10): 73. doi:10.1007/s11892-015-0654-x. PMC 4539350. PMID 26280364. So far, none of the hypotheses accounting for virus-induced beta cell autoimmunity has been supported by stringent evidence in humans, and the involvement of several mechanisms rather than just one is also plausible.
33. Butalia S, Kaplan GG, Khokhar B, Rabi DM (December 2016). "Environmental Risk Factors and Type 1 Diabetes: Past, Present, and Future". *Canadian Journal of Diabetes*(Review). **40** (6): 586–93. doi:10.1016/j.cjcd.2016.05.002. PMID 27545597.
34. Serena G, Camhi S, Sturgeon C, Yan S, Fasano A (August 2015). "The Role of Gluten in Celiac Disease and Type 1 Diabetes". *Nutrients*. **7** (9): 7143–62. doi:10.3390/nu7095329. PMC 4586524. PMID 26343710.
35. Visser J, Rozing J, Sapone A, Lammers K, Fasano A (May 2009). "Tight junctions, intestinal permeability, and autoimmunity: celiac disease and type 1 diabetes paradigms". *Annals of the New York Academy of Sciences*. **1165** (1): 195–205. Bibcode:2009NYASA1165..195V. doi:10.1111/j.1749-6632.2009.04037.x. PMC 2886850. PMID 19538307.
36. Laugesen E, Østergaard JA, Leslie RD (July 2015). "Latent autoimmune diabetes of the adult: current knowledge and uncertainty". *Diabetic Medicine*. **32** (7): 843–52. doi:10.1111/dme.12700. PMC 4676295. PMID 25601320.
37. "Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications"(PDF). World Health Organization. 1999. Archived (PDF) from the original on 2003-03-08.
38. Cleland, S. J.; Fisher, B. M.; Colhoun, H. M.; Sattar, N.; Petrie, J. R. (2013). "Insulin Resistance in Type 1 Diabetes". *Diabetologia*. National Library of Medicine. **56** (7): 1462–1470. doi:10.1007/s00125-013-2904-2. PMC 3671104. PMID 23613085.
39. ^ Unless otherwise specified, reference is: Table 20-5 in Mitchell, Richard Sheppard; Kumar, Vinay; Abbas, Abul K.; Fausto, Nelson (2007). *Robbins Basic Pathology* (8th ed.). Philadelphia: Saunders. ISBN 978-1-4160-2973-1.
40. Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, Seshasai SR, McMurray JJ, Freeman DJ, Jukema JW, Macfarlane PW, Packard CJ, Stott DJ, Westendorp RG, Shepherd J, Davis BR, Pressel SL, Marchioli R, Marfisi RM, Maggioni AP, Tavazzi L, Tognoni G, Kjekshus J, Pedersen TR, Cook TJ, Gotto AM, Clearfield MB, Downs JR, Nakamura H, Ohashi Y, Mizuno K, Ray KK, Ford I (February 2010). "Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials". *Lancet*. **375**(9716): 735–42. doi:10.1016/S0140-6736(09)61965-6. PMID 20167359. S2CID 11544414.
41. "Blood sugar testing: Why, when and how". *mayoclinic.org*. Mayo Foundation for Medical Education and Research. Retrieved 27 April 2017.
42. Jump up to:^{a b} MedlinePlus > Blood glucose monitoring Archived 22 January 2010 at the Wayback Machine Update Date: 6/17/2008. Updated by: Elizabeth H. Holt, MD, PhD. In turn citing: American Diabetes Association. Standards of medical care in diabetes" *Diabetes Care* 2008; 31: S12–54.



43. Li, Rui; Zhang, Ping; Barker, Lawrence E.; Chowdhury, Farah M.; Zhang, Xuanping (1 August 2010). "Cost-Effectiveness of Interventions to Prevent and Control Diabetes Mellitus: A Systematic Review". *Diabetes Care*. **33** (8): 1872–1894. doi:10.2337/dc10-0843. ISSN 0149-5992. PMC 2909081. PMID 20668156.
44. Cowie C.C., Rust K.F., Byrd-Holt D.D., Gregg E.W., Ford E.S., Geiss L.S., Bainbridge K.E., Fradkin J.E. Prevalence of diabetes and high risk for diabetes using hemoglobin A1c criteria in the U.S. population in 1988–2006. *Diabetes Care*. 2010;33:562–568.
45. Narayan K.M., Boyle J.P., Geiss L.S., Saaddine J.B., Thompson T.J. Impact of recent increase in incidence on future diabetes burden: U.S., 2005–2050. *Diabetes Care*. 2006;29:2114–2116.
46. Wild S., Roglic G., Green A., Sicree R., King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047–1053.
47. Gamsey, S.; Bernat, V.; Kutayavin, A.; Clary, J.W.; Pradhan, S. Near-IR glucose sensors. U.S. Patent US20180179233A1, 27 December 2016.
48. Esenaliev, R.O. Noninvasive Blood Glucose Monitoring With Optical Coherence Tomography. *Diabetes Care* 2002, 25, 2263–2267
49. Garg SK, Michels AW, Shah VN. Use of non-insulin therapies for type 1 diabetes. *Diabetes Technol Ther*. 2013;15:901–8.
50. 3. U.K. prospective diabetes study 16. Overview of 6 yers' therapy of type II diabetes: A progressive disease. U.K. Prospective Diabetes Study Group. *Diabetes*. 1995;44:1249–58.
51. 4. Shah VN, Moser EG, Blau A, Dhingra M, Garg SK. The future of basal insulin. *Diabetes Technol Ther*. 2013;15:727–32
52. Huang, Mingzhan, et al. "Modeling impulsive injections of insulin: towards artificial pancreas." *SIAM Journal on Applied Mathematics* 72.5 (2012): 1524-1548.
53. HO YICK WAI, YVONNE AUDREY. "PATIENT-SPECIFIC CONTROLLER FOR AN IMPLANTABLE ARTIFICIAL PANCREAS." (2016).
54. Pickup, John. "Insulin pumps." *Diabetes technology & therapeutics* 16.S1 (2014): S-17.
55. Thompson, Jon S., and William C. Duckworth. "Insulin pumps and glucose regulation." *World journal of surgery* 25.4 (2001): 523.