OVERVIEW OF TYPE 2 DIABETES MELLITUS (T2D)

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After completing my master's, I taught medical biochemistry at Ghana Medical School for 4 years. I was accepted into a PhD program in Canada. I pursued my thesis work at the University of Ottawa, where I earned a doctorate of philosophy in biochemistry.

My 20 years' experience in teaching and in preclinical and clinical research includes cancer chemotherapy, developmental heart defects, and autoimmune kidney diseases which led me to my current profession as a freelance medical writer and editor.

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What is Type 2 Diabetes Mellitus (T2D)?

Type 2 diabetes mellitus (T2D) is a complex, metabolic, chronic disease. It is managed by lifestyle changes including daily exercise, weight loss, changes in diet that include stopping sugared drinks, limiting alcohol as well as smoking cessation and oral and injected medicines.(1,2,3)

Three factors contribute to disease development: a) pancreas lacks insulin production, thereby reducing glucose uptake from the blood into the cells b) the pancreas produces sufficient insulin, but the cells are insensitive to glucose uptake and c) both a and b.

These effects result in high blood glucose (hyperglycemia) which damages blood vessels and, if untreated, leads to disability and premature death.

Cells are the basic units of life, and the body consists of trillions of them; they are specialized to play different roles. Cells need nutrients from foods we eat to maintain our bodies.

A major nutrient cells need is glucose to make energy immediately, and to store some as glycogen for later use. If glucose uptake by cells is perturbed, glucose metabolism is impaired. Thus the disease initially manifests itself as symptoms resulting from hyperglycemia. If cells are unable to take in glucose, proteins are broken down to make glucose.

The causes of T2D differ from type 1 diabetes mellitus (T1D). In individuals living with T1D, their immune system attacks and destroys the pancreatic beta cells and so little or no insulin is produced, so external insulin must be injected.

In contrast, T2D is associated with the cells' inability to respond to available insulin (insulin resistance) and, as the disease progresses, impaired insulin production by the pancreatic beta cells (beta-cell dysfunction).(4)

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Why is high blood glucose a problem if cells have other ways of making energy?

High blood glucose damages the kidney blood vessels and prevents them from cleaning the blood efficiently.(5) These effects cause glucose and proteins to appear in the urine. Ultimately, untreated high blood glucose causes kidney failure, heart attack, blindness and premature death.

Why is T2D also known as non-insulin-dependent or maturity onset?

Until the 1980s, T2D was known as non-insulin-dependent diabetes mellitus (NIDDM) because unlike type 1 diabetes (T1D), individuals diagnosed with T2D were shown to be able to produce insulin. T2D was also known as maturity-onset diabetes (MOD) because until the 1980s, T2D was believed to be a disease for patients over 40 years and T1D believed to be a disease of childhood. These terms became obsolete as understanding of cellular causes of T1D and T2D increased.

In the past 40 years, the number of children with T2D has increased, overtaking the number of children with T1D.(1,2)

What is the role of the pancreas in T2D?

Figure 1 represents a pancreas; a cone-shaped spongy organ lying in the back of stomach, in the curve of the upper part of the small intestine called the duodenum. Scattered throughout the pancreas are islets of Langerhans. A section shows several distinct cell types, including alpha and beta cells, and producing hormones: glucagon and insulin, respectively.(6)

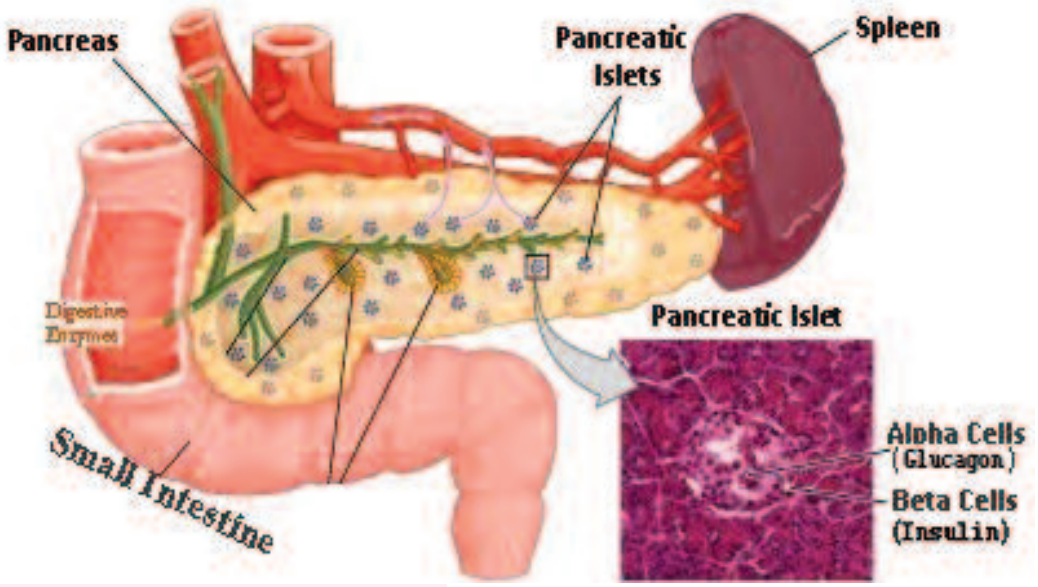
Hormones are chemical messengers that are sent to cells of the body to perform their activities precisely and promptly. These two hormones are regulated and act in an opposing manner to control blood glucose.

Why are cells unable to take in glucose in T2D even if insulin is produced?

In the fed state (after eating), blood glucose concentration rises. In a healthy individual, this signals pancreatic beta cells to produce insulin and release it into the blood so it can travel to where it binds on the outside of cell membranes.

Insulin binds to a protein molecule called its

Figure 1. The pancreas showing the islets of Langerhans. The principal cells of the islets are alpha and beta cells which secrete hormones, glucagon and insulin, respectively. These hormones exhibit opposing effects to regulate blood sugar. After feeding, insulin is secreted from the beta cells into the bloodstream to promote uptake of blood sugar into the liver, muscle, brain and fat cells. In fasting, blood sugar is low, which stimulates glucagon release from the alpha cells and acts by promoting glycogen (stored glucose polymer) breakdown from the cells to increase sugar in blood.(6)



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receptor, and the insulin-receptor complex stimulates processes in the cell membrane which then promote glucose intake from the blood into the cells.

Inside the cell the glucose is used either to make energy or stored for later use. Between meals, at night and during fasting, the blood glucose begins to fall, which in turn, signals glucagon release from the pancreatic alpha cells.

Glucagon then promotes the breakdown of glycogen to glucose to be used by the cells for energy, Figure 2A. In this way, the body maintains its energy status and its important activities.

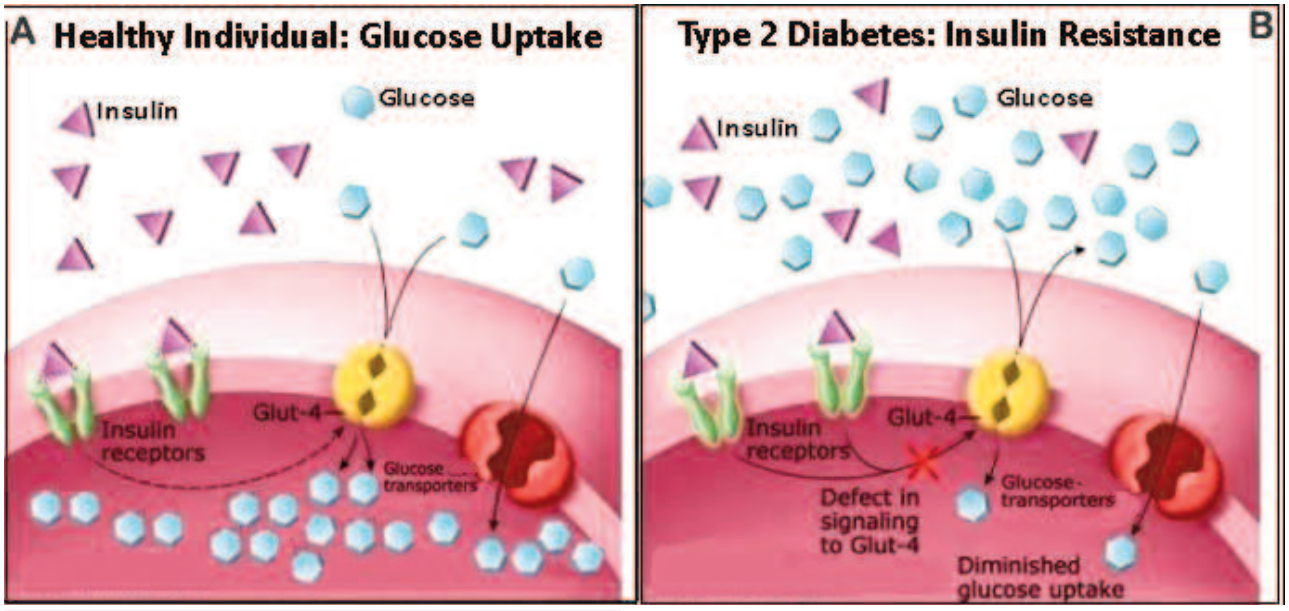
In T2D insulin is produced by the beta cells of the islets ranging from less than normal to greater than normal amounts. This abnormality is not so much to do with insulin production but due to loss of sensitivity in the process leading to glucose uptake by the cells, after insulin binding to its receptor on the cell membrane.(7) This results in glucose build-up in the blood, Figure 2B, a condition called insulin resistance, and it is common in obese individuals.

One characteristic in T2D development is that pancreatic beta cells produce more insulin than is normally needed, as the inability of the cells of the body to react to insulin results in decreased glucose uptake.

The reason for injecting individuals living with T2D with insulin is because as T2D progresses, the pancreas become less able to produce sufficient insulin for normal glucose uptake by the cells of the body.

After digesting a carbohydrate meal, the glucose enters the blood. Figure 3 shows what happens over time if blood samples are taken and tested for glucose from healthy individuals with prediabetes (in between health and diabetes stage) and individuals diagnosed with diabetes. The blood glucose curve in individuals with no symptoms of diabetes peaks at around 120

Figure 2. Glucose uptake normally and in individuals with T2D. A) Normally, insulin is secreted and released into the blood when the blood sugar level rises to promote uptake by the cells. Thus insulin brings the sugar levels down to normal. B) In individuals with T2D, the cells are insensitive to sugar uptake, even if insulin has been secreted and released by the beta cells, resulting in sugar accumulation at high levels in the blood (hyperglycemia). Modified from Tsatsoulis et al.(7)



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mg/dL, because the glucose is rapidly taken up by the cells.

In individuals with prediabetes, blood sugar measurements indicate mild insulin resistance. Their glucose uptake is not efficient, resulting in the moderate build-up in the blood with a peak of as much as 190 mg/dL.(7-9)

This prediabetic value has not reached the extent that will be harmful to the body. In untreated diabetes, blood glucose can rise as high as 360 mg/dL which can cause complications such as kidney failure, heart attack, coma and early death.

Insulin resistance

The mechanisms underlying impaired insulin secretion or insulin-receptor complex malfunction in glucose uptake is unclear, but the prediction is that both genetic and environmental factors, as well as, hormone imbalance might play a role. Our body's activities depend on how much of a particular substance is there (substance levels).(5)

In normal production of insulin, but lowered sensitivity of the insulin-receptor complex to the glucose uptake process, one or more of the factors downstream or beyond the initial insulin-receptor binding might be defective, as you will see with Glut-4 signaling in the glucose uptake model in Figure 2.

Genetic factors

T2D runs in families. Genetic studies have identified around 65 genetic variants on different chromosomes, mostly mapped as high-risk factors in T2D.(10-17)

Some genetic variants cause impaired beta cell function and so reduces insulin production, or affects how insulin works, deregulation of the cell cycle (the cycle that leads to cell growth and specialization), brain function (CNS neurotransmission), insulin-release competent genes and immune system regulatory genes.(11,12,13)

Depending on which genetic variants individuals inherit from their ancestors, they can be at high or low risk for T2D.(14)

Those with high-risk genetic variants may have increased body mass index (BMI).(12,14)

BMI is a measurement of our body fat, and it depends on each individual's height and weight.

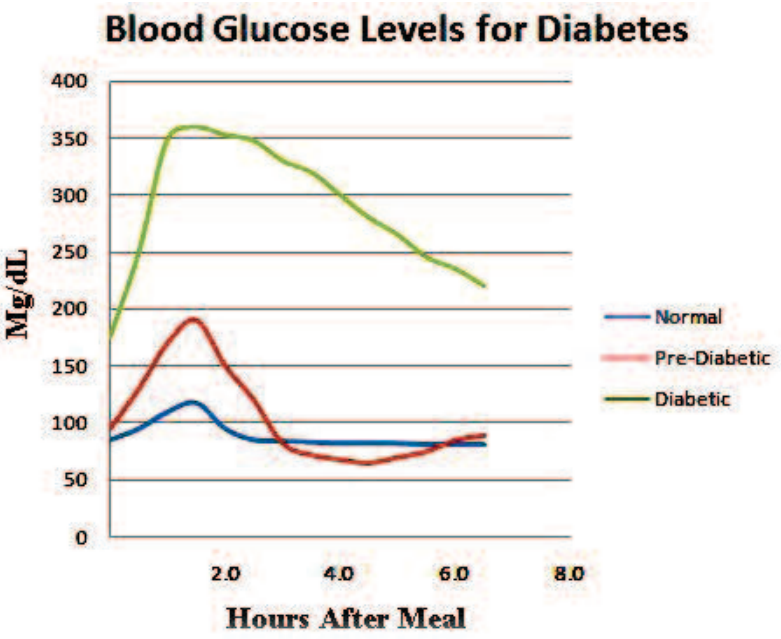

Figure 3.

Six-hour time course of blood glucose concentration after a meal.

Normal blood glucose curve (blue) peaked at 120 mg/dL at 1 h.

Prediabetes blood glucose curve (red) peaked at 190 mg/dL, while diabetes blood glucose curve (green) peaked at 360 mg/dL around the same time (1 h).(9)

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Environmental factors

Apart from the involvement of genetic factors, scientists have shown that individuals who have inherited high-risk genetic variants are susceptible or sensitive to environmental factors that cause excessive weight gain (obese).

Scientists have reported that exposure to chemicals containing compounds like phthalates and bisphenol A, contained in some body care products can disrupt body hormones additional to glucagon and insulin.(18,19) This effect can trigger obesity which can, in some individuals, result in T2D.

Additionally, lack of physical activity, poor or imbalanced diets, and sugary drinks: these all worsen health and hasten the onset of complications of T2D.

High blood pressure, high cellular release of triglycerides (fat), as well as, lifestyle habits such as persistent alcohol use, smoking, and recreational drug use can accelerate T2D progression.

Finally, aging may contribute to T2D development, and the reason might be, in part, due to prolonged exposure to pollutants.

Hormone imbalance due to stress

Studies have shown that persistent stress, caused by so many factors such as trauma, poverty, discrimination, work overload, and so on, are external stimuli that can lead to physiological and psychological responses to the production of several hormones of the body.

These hormones include cortisol and epinephrine, which prepare the body for fight-or-flight (defend or run away), thus cause a rise in blood glucose, and could consequently overwhelm the regulatory systems responsible for balancing blood sugar levels, with ultimate high blood pressure and insulin resistance.(20)

Affected individuals with T2D in the USA

According to the American Diabetes Association statistics, T2D ranks #7 leading cause of death in the United States and the prevalence in the USA population 2012 was 29.1 million individuals.(21)

Symptoms of T2D

T2D development is gradual, and because of this the signs and symptoms are hard to tell from the beginning.

It is possible to have the disease for several years without knowing, which is why providing an accurate family history and early screening is important, especially if one is a high-risk individual.

Typical T2D symptoms:

-Feeling too tired (fatigue) and weak because the cells could not uptake sugar and use it for energy and had been mimicking a condition of glucose deprivation.

-The fluid loss makes individuals with T2D feel thirsty. They tend to drink more because of loss of fluid from cells of the body. Feeling thirsty is the body's attempt to balance the high concentration of glucose in the blood.

-Individuals with T2D pass water (pee) persistently because of frequent drinking of fluids.

-Feeling hungry all the time. Because glucose is built-up in the blood, and since it is not in use by the cells, they mimic a situation of glucose deprivation.

-Kidney damage. When the blood glucose is too high, kidneys cannot handle the filtration and glucose appears in the urine, glycosuria.

-Weight loss. Obesity is a risk factor for development of T2D, but due to a persistent lack of glucose in the cells as the disease develops, the body finds alternative ways of generating energy such as the use of more stored fat and muscle proteins and the outcome is weight loss.

-Cannot see properly (blurry vision). Eye lenses lose water due to the blood glucose build-up, resulting in impaired focusing.

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-Wounds or sores take a long time to heal. Besides, wounds can very quickly catch infection which might be due to the perturbed brain and immune system activities.

-Dark skin patches are observable in folded areas of the skin, such as the neck and armpit regions.

-Drowsiness. Feelings of drowsiness from lack of energy.

Signs of T2D complications

Complications arise when diabetes is untreated or poorly controlled. T2D mismanagement often occurs, especially, at early stages of the disease when there are minimal symptoms.

If ignored for a lengthy period, T2D impairs several vital organs of the body resulting in more health disaster, as indicated below:

-Fruity or wine-smelling odor occurs because of excessive usage of fat for energy, which is due to a cellular deprivation of glucose. More than usual fat catabolism produces a by-product called ketones which have this kind of smell.(22)

-Diabetic ketoacidosis occurs when a T2D patient, in addition to fruity-odor-breath, also has symptoms such as nausea, vomiting, abdominal pain and deep or heavy breathing, and is a result of prolonged and excessive fat usage when a patient ignores the treatment of initial symptoms.(22)

-Heart and blood vessel damage can occur, which can cause coronary heart disease (CHD); a block in the blood vessel that nourishes the heart. Subsequently, heart failure, stroke, high blood pressure and obstruction of blood flow through the arteries (atherosclerosis) due to fat clogging may occur.

-Nerve injury caused by high glucose level which hurt the walls of tiny blood vessels (capillaries) that nourish the nerves. The nerves localized in the legs, in particular, when injured, can cause pain and if they ultimately get damaged, it causes numbness, with no feelings in the legs and toes.(23)

-Leg tissue damage results from nerve injury, or diminished blood flow through the leg.

-Lower limb amputation results from circulation cut off to the feet, and death of the leg muscles.

-Kidney damage, eye damage and hearing impairment occurs because excess blood glucose damages the blood vessels.(4)

There is a greater risk of triggering Alzheimer's disease (AD) because of complications such as damage to the brain blood vessels and subsequent decreased blood flow to the brain, resulting in dementia and cognitive problems similar to symptoms observed in AD.(24) This complication can arise from prolonged mismanagement of T2D. Also, some regulatory genes common to the development of both T2D and AD might exhibit impaired function.

Lack of proper care of T2D can enhance development and progression (growth and spread) of cancer due to insulin resistance, high blood insulin (hyperinsulinemia due to insulin medications), and high circulating lipids (hyperlipidemia).(25-27)

Studies have shown that these excessive circulating substances in the blood results in elevated levels of insulin growth factor (IGF) which can contribute to the development of cancer.(25-27)

In extreme cases diabetic coma or unconsciousness occurs as a result of excessively high blood glucose levels (hyperglycemia) without treatment and can be fatal, leading to brain damage and subsequent death. However, more frequently, unconsciousness comes from is low blood suagr caused by not eating enough after injecting insulin or taking oral medicines.

Is T2D reversible?

Yes, T2D can go away and never return (remission) in some patients who make drastic lifestyle changes early after diagnosis, eg, entirely eliminate sugary drinks, when the vital

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organs of the body are still able to function normally.

It is crucial that they practice their new habits such as administering new medication, sticking with the diabetic dietary plan, exercise regularly, cut down on the caloric intake to 1,200-1,800 calories/day, no smoking, and no alcohol, as well as attending support programs.

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Patients diagnosed with T2M are trained by diabetes educators on how to manage treatment of their disease.

Download a presentation by Dr Sackey from
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