Type 1 Diabetes Mellitus

A Biomedical Summary

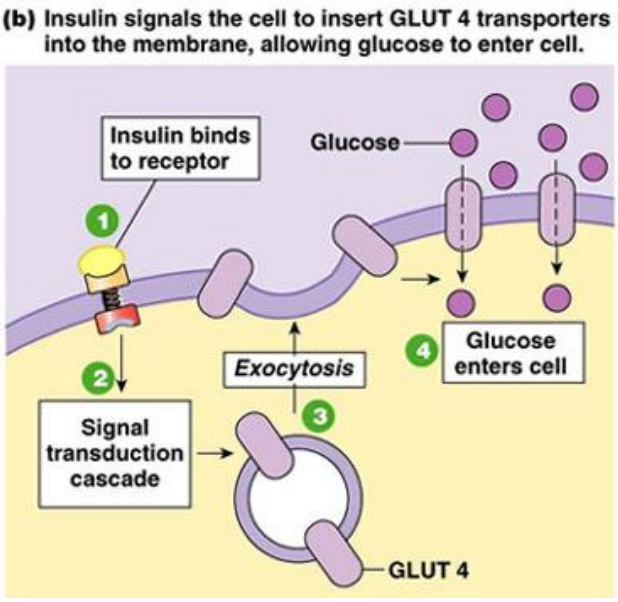
By: Sarah A. Johanson

Diabetes Mellitus (DM) is defined as a chronic disorder of the metabolism which is characterized by a deficiency, either relative or absolute, of the hormone insulin. There are many types of DM; type 1 and type 2 DM being the most common. In this biomedical summary, I will be discussing type 1 DM: What are the characteristics of type 1 DM? What causes type 1 DM? Finally; what complications result?

1. Characteristics

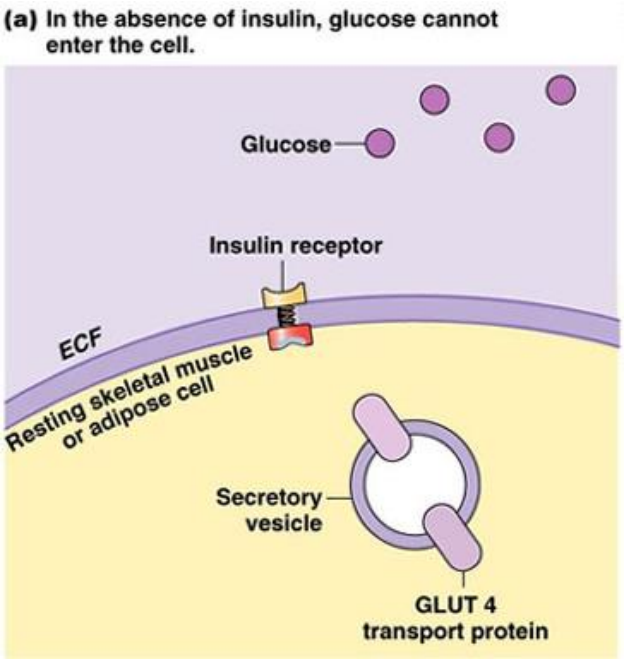
Type 1 Diabetes Mellitus, commonly referred to as insulin-dependent diabetes mellitus (IDDM), is a chronic condition in which the pancreas produces little to no insulin. Onset of IDDM is typically in childhood and adolescence, with peaking incidence at 10 to 12 years of age, but can be at any age.

1.1 The Role of Insulin



Insulin is a peptide hormone produced by beta cells in the pancreas. The role of insulin is to regulate the metabolism of carbohydrates, proteins and fats, primarily by facilitating the entry of substances into the cell. Insulin is necessary for the entry of glucose into the muscle and fat cells, prevention of mobilization of fats from fat cells, and storage of glucose as glycogen in the cells of the liver and muscle.

The chemical composition and molecular structure of insulin are such that it fits into receptor sites on the cell membrane. Here, it initiates a sequence of chemical reactions that alter the membrane of the cell to facilitate the entry of glucose into the cell and also to stimulate enzymatic systems outside the cell that metabolize the glucose for energy production.



In IDDM, when insulin is deficient, glucose is unable to enter the cell, and its concentration gradually builds up in the bloodstream. This increased concentration of glucose, hyperglycemia, produces an osmotic gradient that causes the movement of body fluid from the intracellular space to the interstitial space then to the extracellular space and finally into the glomerular filtrate in order to “dilute” the hyperosmolar filtrate.

1.2 Symptoms

Common symptoms of IDDM include:

- Excessive urination (polyuria); results from the kidneys attempting to rid the body of excess glucose in the blood.
- Increased thirst (polydipsia); due to the loss of water and electrolytes through excessive urination.
- Dry mouth (xerostomia); due to dehydration.
- Increased Hunger (polyphagia); due to energy from glucose being lost through urination.
- Blurry vision; due to glucose build up in the lens of the eye. Extra water is sucked into the eye, resulting in changes in the lens shape.
- Unintentional weight loss; due to loss of glucose (calories) through urination, and through dehydration.
- Fatigue; due to malabsorption of energy from glucose.

2. Causes

IDDM is currently believed to be an auto immune disease that arises when a person with a genetic predisposition is exposed to a precipitating event; usually a viral infection. IDDM is not inherited, however, heredity is unquestionably a prominent factor in the etiology. It appears that susceptibility to IDDM depends on a locus within the human lymphocyte antigen (HLA) complex. Antibodies to some aspect of islet tissue are regularly present at the time of diagnosis. Pancreatic cell antibodies (ICA's) are found in about 70%-85% of patients that are newly diagnosed. They usually disappear by one year after diagnosis, but in some people, they may persist for years.

2.1 Human Leukocyte Antigen

The human leukocyte antigen (HLA) system is the location of genes that encode for proteins on the surface of cells that are responsible for the regulation of the immune system. This group of genes is located on chromosome 6. HLA's corresponding to the MHC class 2 (DP, DM, DOA, DQ, and DR) present antigens from outside of the cell to T-lymphocytes. These antigens stimulate the multiplication of T-helper cells, which in turn stimulate antibody-producing B-cells to produce antibodies to that specific antigen.

2.2 Current Theories

The current theory is that the presence of HLA genes causes a defect in the immune system that renders the person susceptible to a trigger event, which is usually a virus, but can also be bacteria or a chemical irritant. In DR3-positive persons, the virus invades the beta cells and initiates an autoimmune process that gradually destroys them. Without beta cells, no insulin can be produced.

Controversy exists as to whether the autoimmune response is primarily mediated by the lymphocyte response or the antibody response or is a result of the two. A variety of viruses have been implicated as the prime environmental factor in the onset of DM including; the Epstein-Barr virus, Coxsackie virus, mumps virus, and cytomegalovirus.

3. Complications

Long-term complications of IDDM develop gradually, but can affect major organs in the body, including, heart, blood vessels, nerves, eyes and kidneys.

- **Heart and blood vessel disease:** IDDM dramatically increases risk of cardiovascular problems such as coronary artery disease with chest pain (angina), heart attack, stroke, narrowing of the arteries (atherosclerosis) and high blood pressure.

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- **Nerve damage** (neuropathy): excess glucose can injure the walls of the capillaries that nourish the nerves. Poorly controlled blood sugar can result in lost sense of feeling in affected limbs.
- **Kidney damage** (nephropathy): the kidney is responsible for filtering waste from the blood. DM can damage this filtration system, resulting in kidney failure or kidney disease.
- **Eye damage**: DM can damage the blood vessels of the retina, potentially leading to blindness.
- **Foot damage**: nerve damage or poor blood flow to the feet can ultimately lead to serious infections, which may require amputation of limbs.
- **Skin and mouth conditions**: DM increases risk for skin problems, including bacterial and fungal infections.
- **Pregnancy complications**: High blood sugar levels can be dangerous and may increase risk for miscarriage, stillbirth and birth defects. For the mother, DM increases risk for diabetic ketoacidosis, retinopathy, pregnancy-induced high blood pressure and preeclampsia.

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Type 1 and Type 2 Diabetes

What are Type 1 and Type 2 diabetes? What can cure them? And what can be done to prevent diabetes completely? As the topic of diabetes is discussed all three of the questions will be answered. First, what are Type 1 and 2 diabetes? In type one, the body's beta cell groups are attacked by misguided immune cells causing the insulin to fail in receiving the glucose needed to store energy in the liver and muscles. In type two, the body's insulin receptors are unable to connect to give of a charge, which in turn would tell the glucose channels to open. When failing to do so the glucose stays in the bloodstream, raising the blood sugar. Many people across the world have diabetes and the medication, up until the 1980's, was pig insulin. Yet since then, Doctors have been able to find a way to use pure human insulin for treatments.

In the human body beta cells form together islets. The islets then create insulin which is released into the passing bloodstreams. Then the bloodstreams carry the insulin to three main areas; the liver, fat, and muscle tissue where they signal receptors to open up and take in the glucose. The liver, fat, and muscles take in the glucose and use it as an energy source. When a young adult generates type one diabetes, the immune cells in the body attack the beta cells, causing the islets to lose most of the ability to create insulin when glucose is released, causing the bloodstream to carry a high amount of glucose to the targeted areas. When adults experience type two diabetes, the result is high levels of glucose. Upon reaching their destination with little to no insulin to signal

to the receptors, the bloodstream has no choice but to carry around energy that soon raises the body's blood sugar. When the bloodstream has high blood sugar nerves and tissues are damaged, leaving the patient with deteriorating health if not cured.

In the 1900's doctors found a way to take insulin from pig and cow pancreas's and purify it, so much so that the human body will accept the pig or cow insulin. The body's lacking ability to create insulin is helped by the foreign animal's insulin to send signals toward the glucose receptors so it can take up the glucose. Yet in the 1980's doctors were able to purify human insulin to a point where any patient's body is able to accept the insulin needed. In type two diabetes the signals are not existing in the cells. When insulin is injected into the bloodstream it opens up the insulin-receptors so that the charge is available for the glucose receptors to intake the glucose cells.

When a patient is diagnosed with either type one or type two diabetes, doctors recommend a special diet to achieve a balanced level blood sugar. The different types of foods that are essential to diabetic patients are: Whole grains, whole oats, Omega-3 (which is found in fishes), beans, apples, broccoli, and nuts. Plenty of water and low fat foods are key items to have. When wanting a snack low-fat cheese, sugar-free Jell-O, avocado, and eggs are a great and safe way to get the low amounts of proteins and carbs a patient would need.

What are Type 1 and Type 2 diabetes? Type one, the immune cells attack beta cells, causing the islets to lose the ability to create insulin. Type two, little to no insulin is available to signal the receptors, the bloodstream has no choice but to carry around energy raises the blood sugar. Causing the nerves and muscle tissues to be damaged. What can cure them? Purified insulin from pigs, cows, and even human pancreas's. And what can be done to prevent diabetes completely? Eating a healthy diet. But if someone is diagnosed, eating low-carb and low-sugar foods is essential.

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"What Causes the Immune System to Destroy the Beta Cells in Type 1 Diabetes Patients"

Ben Martin 10/22/15

Type one diabetes affects only 5% of those diagnosed with diabetes. With around 200,000 cases a year, this is a common disease. Type one diabetes is normally detected in young children and teens but it occurs later in adult life. It normally affects 14 to 60 year olds but all ages are susceptible to the disease.

Type one diabetes is caused when the white blood cells mistakenly attack, and destroy, most of the insulin producing beta cells located in the pancreas. Beta cells are unique cells that produce, store, and distribute the hormone insulin. Insulin is a hormone secreted by the body to help eliminate extra glucose in the body by either burning it off as energy or storing it for later use in the pancreas. After the immune system attacks the beta cells, the remaining cells do not produce enough insulin to keep the body's glucose level balanced. This causes a massive amounts of glucose to build up around in the body, raising the patient's blood sugar to dangerous levels. The high blood sugar causes a myriad of problems including the destruction of tissues throughout the body due to an insufficient amount of insulin available to "feed" the glucose hungry cells. The high blood sugar also causes organ damage to the eyes, liver, spleen, and kidneys. Type one also can cause stroke and heart attacks due to the hardening of the arteries.

Currently, no treatment exists for Type one diabetes and it is considered a chronic illness. If you have Type one diabetes you will need multiple injections of insulin a day, typically within 10 minutes of finishing a meal, and a massive cut back on the consumption of sugary foods. And they must keep a carful track of their blood sugar, this is done by pricking their finger several times a day and that blood is placed on a small portable meter. By taking these steps diabetes patients vastly improve their quality of life.

Recent research conducted by the *National Institute of Health, Diabetes, Digestive, and Kidney Diseases*, released a report on Type one diabetes and the possible causes of Type one. The following is an excerpt from that article:

> "Viruses and infections. A virus cannot cause diabetes on its own, but people are sometimes diagnosed with type 1 diabetes during or after a viral infection, suggesting a link between the two. Also, the onset of type 1 diabetes occurs more frequently during the winter when viral infections are more common. Viruses possibly associated with type 1 diabetes include coxsackievirus B, cytomegalovirus, adenovirus, rubella, and mumps. Scientists have described several ways these viruses may damage or destroy beta cells or possibly trigger an autoimmune response in susceptible people. For example, anti-islet antibodies have been found in patients with congenital rubella syndrome, and cytomegalovirus has been associated with significant beta cell damage and acute pancreatitis—inflammation of the pancreas. Scientists are trying to identify a virus that can cause type 1 diabetes so that a vaccine might be developed to prevent the disease."[1]

[1] NIH Publication No. 14–5164 June 2014

This article sheds a light on the hopes of finding a vaccine against, or at least mitigate, the progression of Type one diabetes and the possibility of stopping it in the future.

Another treatment option for Type one is replacing the dead beta cell islets with donor islets in the hope that the body doesn't recognize those beta cells as intruders, thus providing the body with a larger amount of insulin production. This currently a theory[2] and is being tested if it is a viable treatment option for diabetes.

The use of the entire pancreas as a vehicle for transporting beta cell islets to the body of a diabetic[3]. This treatment is commonly used with patients who have very severe cases of Type one diabetes. If the body accepts the new organ, the new person will no longer need insulin shots, they can eat a normal diet, and start to reverse diabetes in them. Due to the high risk of the body rejecting (when the body does not recognize the new pancreas and it will not use it) the new organ. Patients with the new organ must take drugs to keep the body from rejecting the new pancreas.

Why the white blood cell turns on its own friendly beta cells remained a mystery. Until early in 2015 when a group of British scientists from Monash University[4] discovered when a white blood cell's receptor bonds to an immune cell in an inverse way; the immune cell gives off a signal that tells the white blood cells in the area that the immune cell is infected. This results in that cell being destroyed by the immune system. This theory suggests that it is the orientation of bonding cells which emit a distress call and tells the immune system to destroy all of the "distressed" cells.

Just because you have diabetes doesn't mean that one cannot have a good quality of life. You can most definitely live a happy and fulfilling life while managing diabetes. These future treatment options, and hopeful discovery of a vaccine, will make living with diabetes even easier in the future

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An Executive Summary of Diabetes Mellitus Type 1

By Isabel Kosic

Diabetes mellitus type 1 (also known as type 1 diabetes, and formerly known as both insulin-dependent diabetes and juvenile diabetes) is an autoimmune condition. An autoimmune condition means a person's immune system mistakes the cells in his or her own body as harmful and attacks these cells, destroying them completely or damaging them. The immune system of someone with type 1 diabetes will destroy beta cells in a certain part of the pancreas called the islet tissue. Insulin is produced by these targeted beta cells.

A person with type 1 diabetes is unable to make his or her own insulin. This leads to the person having to get insulin injections to somewhat control the blood sugar in his or her body, but these insulin injections cannot control the amount of blood sugar as well as the pancreas would.

The exact cause of type 1 diabetes is unknown, but researchers have found that several factors can contribute in the appearance of type 1 diabetes.

Type 1 diabetes is often inherited. The risk of a child developing type 1 diabetes is about 10% if his/her father or sibling has diabetes. If the child's mother has diabetes, the risk for the child to get type 1 diabetes is 1%-4%. The risk for people who do not have a close relative with type 1 diabetes is about 0.5%.

There is also theory that proposes that type 1 diabetes is a virus-triggered autoimmune response in which the immune system attacks virus-infected cells along with beta cells in the pancreas. Also, it is believed that certain drugs and chemicals destroy cells in the pancreas.

Currently, there is no way to prevent type 1 diabetes, but ongoing studies are being conducted, and exploring ways to prevent diabetes in those who are most likely to get it.

Modern treatment options for type 2 diabetes

by Ned Stanley

There are 3 treatment options for type 2 diabetes. The first option is dieting with exercise; second is use of prescription drugs; and finally, a combination of both. Each option has its limitations.

Option one consists of dieting along with exercise. The purpose of dieting is to control the intake of fats, carbohydrates and proteins. Dieting is paired with exercise such as walking or tennis. The goal is to create an active lifestyle where food intake is balanced with aerobic exercise. Proper dieting and exercise helps stabilize blood sugar closer to normal levels so that the patient does not need to rely on medication. This option is limited to less severe cases of type 2 diabetes. The treatment is self administered through a healthier lifestyle.

The second treatment option is the use of powerful drugs / medications that are used to control the diabetes. This treatment includes the doses of “Metformin, Sulfonylureas, Meglitinides, Thiazolidinediones, Pioglitazone, etc. These medications have side effects that include but are not limited to: “Bloating, diarrhea, upset stomach, constipation, abdominal pain, nausea, low blood glucose, skin rash, irritability, headache, sore throat, stuffy nose, upper respiratory infection, edema, and increased risk of congestive heart failure. The patient usually requires frequent checkups to ensure the medication is working properly. Medications are helpful for patients with more advanced diabetes or may have difficulty living a healthy lifestyle.

The third and most common option combining diet and exercise with medication. The plan is often used because a patient’s diabetes cannot manage their diabetes alone and reqire the additional blood sugar regulators of medications. These patients are typically have more advanced diabetes but controllable with diet, exercise, and medication.

If patients are unable / unwilling to manage their diabetes with a healthy lifestyle / diet and limited medications. Then they ma advance to requiring regular insulin. Insulin is the last line of defense against uncontrollable blood sugar levels.

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