Diabetes Mellitus and Its Management

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***Abstract*—What causes diabetes? Diabetes happens when our body does not make insulin. This can be because our body does not make any insulin at all, or it does not make enough insulin for what our body needs. Sometimes our body makes insulin. It is not good insulin. Another reason is that our cells are not able to use insulin. This leads to a lot of sugar in our blood. That is what causes diabetes. [1] The problem with cells not using insulin properly affects the cells in our muscles and fat. This is called insulin resistance. Insulin resistance is the problem in type 2 diabetes. In type 1 diabetes, our body does not make any insulin because the cells in our pancreas that make insulin are damaged. In type 2 diabetes, these cells get damaged over time. That makes our blood sugar levels go up. [2]**

We get a type of sugar called glucose from food. Our body needs glucose to have energy. When we eat our body, breaks down the carbohydrates into glucose. The glucose goes into our bloodstream. Then to all the cells in our body. Glucose needs help to get into our cells. That is where insulin comes in. Insulin helps glucose get into our cells. Without diabetes insulin, our cells do not get the glucose they need even if there is a lot of glucose in our blood. This can happen in some types of diabetes. It is like our cells are starving even though there is a lot of glucose around. Our body gets rid of the glucose by putting it in our urine. Diabetes is a condition that happens when our body has a lot of glucose in the blood. [3]

Our body needs glucose to work properly. We need insulin to help the glucose get into our cells. Without insulin, we would not be able to use the glucose we get from food. That is why insulin is so important for people with diabetes. Diabetes is a condition. We can learn more, about diabetes by reading about insulin resistance and diabetes. [4]

I. INTRODUCTION

- What is Diabetes? Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels, which result from defects in insulin secretion, or action, or both. Diabetes mellitus, commonly referred to as diabetes (and in this article will be referred to as "diabetes"), was first identified as a disease associated with "sweet urine," and excessive muscle loss in the ancient world. Elevated levels of blood glucose (hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine. Normally, blood glucose levels are tightly controlled by insulin, a hormone produced by the pancreas. Insulin lowers the blood glucose level. When the blood glucose elevates (for example, after eating food), insulin is released from the pancreas to normalize the glucose level. [5]

Fig No 1: What Is Diabetes

- What is the impact of diabetes?

Over time, diabetes can lead to blindness, kidney failure, and nerve damage. Diabetes is also an important factor in accelerating the hardening and narrowing of the arteries (atherosclerosis), leading to strokes, coronary heart disease, and other blood vessel diseases. Diabetes affects 15 million people (about 8% of the population) in the United States. In addition, an estimated 12 million people in the United States have diabetes and don't even know it. From an economic

perspective, the total annual economic cost of diabetes in 1997 was estimated to be 98 billion dollars in the United States. Diabetes is the third leading cause of death in the United States after heart disease and cancer. [6]

• What causes diabetes?

Insufficient production of insulin (either absolutely or relative to the body's needs), production of defective insulin (which is uncommon), or the inability of cells to use insulin properly and efficiently leads to hyperglycemia and diabetes. This latter condition affects mostly the cells of muscle and fat tissues, and results in a condition known as "insulin resistance." This is the primary problem in type 2 diabetes. The absolute lack of insulin, usually secondary to a destructive process affecting the insulin producing beta cells in the pancreas, is the main disorder in type 1 diabetes. In type 2 diabetes, there also is a steady decline of beta cells that adds to the process of elevated blood sugars. For more, please read the Insulin Resistance article2 . [7]

Glucose is a simple sugar found in food. Glucose is an essential nutrient that provides energy for the proper functioning of the body cells. Carbohydratesare broken down in the small intestine and the glucose in digested food is then absorbed by the intestinal cells into the bloodstream, and is carried by the bloodstream to all the cells in the body where it is utilized. However, glucose cannot enter the cells alone and needs insulin to aid in its transport into the cells. Without insulin, the cells become starved of glucose energy despite the presence of abundant glucose in the bloodstream. In certain types of diabetes, the cells' inability to utilize glucose gives rise to the ironic situation of "starvation in the midst of plenty". The abundant, unutilized glucose is wastefully excreted in the urine. [8]

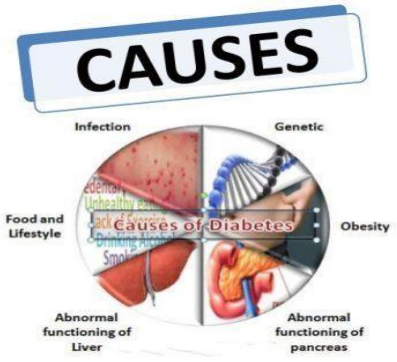

Fig No 2: Causes of Diabetes

Insulin is a hormone that is produced by specialized cells (beta cells) of the pancreas. (The pancreas is a deep-seated organ in the abdomen located behind the stomach.) In addition to helping glucose enter the cells, insulin is also important in tightly regulating the level of glucose in the blood. After a meal, the blood glucose level rises. [9]

• What are the different types of diabetes?

There are two major types of diabetes

1. Type 1
2. Type 2.

Type 1- diabetes was also called insulin dependent diabetes mellitus (IDDM), or juvenile onset diabetes mellitus. In type 1 diabetes, the pancreas undergoes an autoimmune attack by the body itself, and is rendered incapable of making insulin. Abnormal antibodies have been found in the majority of patients with type 1 diabetes. Antibodies are proteins in the blood that are part of the body's immune system. The patient with type 1 diabetes must rely on insulin medication for survival4 . In autoimmune diseases, such as type 1 diabetes, the immune system mistakenly manufactures antibodies and inflammatory cells that are directed against and cause damage to patients' own body tissues. It is believed that the tendency to develop these abnormal antibodies in type 1 diabetes is, in part, genetically inherited, though the details are not fully understood. (Exposure to certain viral infections (mumps and Coxsackie viruses) or other environmental toxins may serve to trigger abnormal antibody responses that cause damage to the pancreas cells where insulin is made. These antibodies can be measured in the majority of patients, and may help determine which individuals are at risk for developing type 1 diabetes. [10]

Type 2- diabetes was also referred to as non-insulin dependent diabetes mellitus (NIDDM), or adult on set diabetes mellitus (AODM). In type 2 diabetes, patients can still produce insulin, but do so relatively inadequately for their body's needs, particularly in the face of insulin resistance as discussed above. In many cases this actually means the pancreas produces larger than normal quantities of insulin. A major feature of type 2 diabetes is a lack of sensitivity to insulin by the cells of the body (particularly fat and muscle cells). Thus, larger quantities of insulin are produced as an attempt to get these cells to recognize that insulin is, in fact, presen In addition to the problems with an increase in insulin resistance, the release of insulin by

the pancreas may also be defective and suboptimal. In fact, there is a known steady decline in beta cell production of insulin in type 2 diabetes that contributes to worsening glucose control. (This is a major factor for many patients with type 2 diabetes who ultimately require insulin therapy.) Finally, the liver in these patients continues to produce glucose through a process called gluconeogenesis despite elevated glucose levels. This control of gluconeogenesis becomes compromised. [11]

- What are diabetes symptoms?

The early symptoms of untreated diabetes are related to elevated blood sugar levels, and loss of glucose in the urine. High amounts of glucose in the urine can cause increased urine output and lead to dehydration. Dehydration causes increased thirst and water consumption. The inability to utilize glucose energy eventually leads to weight loss despite an increase in appetite. Some untreated diabetes patients also complain of fatigue, nausea and vomiting. Patients with diabetes are prone to developing infections of the bladder, skin, and vaginal areas. Fluctuations in blood glucose levels can lead to blurred vision. Extremely elevated glucose levels can lead to lethargy and coma (diabetic coma). [12]

- How is diabetes diagnosed?

The fasting blood glucose (sugar) test is the preferred way to diagnose diabetes. It is easy to perform and convenient. After the person has fasted overnight (at least 8 hours), a single sample of blood is drawn and sent to the laboratory for analysis. Normal fasting plasma glucose levels are less than 100 milligrams per deciliter (mg/dl). Fasting plasma glucose levels of more than 126 mg/dl on two or more tests on different days indicate diabetes. If the overnight fasting blood glucose is greater than 126 mg/dl on two different tests on different days, the diagnosis of diabetes is made. A random blood glucose test can also be used to diagnose diabetes. Random blood samples (if taken shortly after eating or drinking) may be used to test for diabetes when symptoms are present. A blood glucose level of 200 mg/dl or higher indicates diabetes, but it must be reconfirmed on another day with a fasting plasma6 glucose or an oral glucose tolerance test. When fasting a blood glucose stays above 100mg/dl, but in the range of 100-126mg/dl, this is known as impaired fasting glucose (IFG). While patients with IFG do not have the diagnosis of diabetes, this condition carries with it its own risks and concerns, and is addressed elsewhere. [13]

- The oral glucose tolerance test

Though not routinely used anymore, the oral glucose tolerance test (OGTT) is a gold standard for making the diagnosis of type 2 diabetes. It is still commonly used for diagnosing gestational diabetes. With an oral glucose tolerance test, the person fasts overnight (at least 8 but not more than 16 hours). Then first, the fasting plasma glucose is tested. After this test, the person receives 75 grams of glucose (100 grams for pregnant women). There are several methods employed by obstetricians to do this test, but the one described here is standard. Usually, the glucose is in a sweettasting liquid that the person drinks. Blood samples are taken at specific intervals to measure the blood glucose. [14]

- Evaluating the results of the oral glucose tolerance test

Glucose tolerance tests may lead to one of the following diagnoses:

Normal response: A person is said to have a normal response when the 2-hour glucose level is less than 140 mg/dl, and all values between 0 and 2 hours are less than 200 mg/dl. Impaired glucose tolerance: A person is said to have impaired glucose tolerance when the fasting plasma glucose is less than 126 mg/dl and the 2-hour glucose level is between 140 and 199 mg/dl. [15]

Diabetes: A person has diabetes when two diagnostic tests done on different days show that the blood glucose level is high. [16]

Gestational diabetes: A woman has gestational diabetes when she has any two of the following: a 100g OGTT, a fasting plasma glucose of more than 95 mg/dl, a 1-hour glucose level of more than 180 mg/dl, a 2-hour glucose level of more than 155 mg/dl, or a 3-hour glucose level of more than 140 mg/dl [17]

• Why is blood sugar checked at home?

Home blood sugar (glucose) testing is an important part of controlling blood sugar. One important goal of diabetes treatment is to keep the blood glucose levels near the normal range of 70 to 120 mg/dl before meals and under 140 mg/dl at 2 hours after eating. Blood glucose levels are usually tested before and after meals, and at bedtime. The blood sugar level is

typically determined by pricking a fingertip with a lancing device and applying the blood to a glucose meter, which reads the value. There are many meters on the market, for example, Accu-Check Advantage, One Touch Ultra, Sure Step and Freestyle. Each meter has its own advantages and disadvantages (some use less blood, some have a larger digital readout, some take a shorter time to give you results, etc). The test results are then used to help patients make adjustments in medications, diets, and physical activities.There are some interesting developments in home blood glucose monitoring. [18]

Hemoglobin A1c (A1c) To explain what an A1c is, think in simple terms. Sugar sticks, and when it's around for a long time, it's harder to get it off. In the body, sugar sticks too, particularly to proteins. The red blood cells that circulate in the body live for about 3 months before they die off. When sugar sticks to these cells, it gives us an idea of how much sugar is around for the preceding 3 months. In most labs, the normal range is 45.9 %. [19]

In poorly controlled diabetes, its 8.0% or above, and in well controlled patients it's less than 7.0%. The benefits of measuring A1c is that is gives a more reasonable view of what's happening over the course of time (3 months), and the value does not bounce as much as finger stick blood sugar measurements. There is a correlation between A1c levels and average blood sugar levels as follows. While there are no guidelines to use A1c as a screening tool, it gives a physician a good idea that someone is diabetic if the value is elevated. Right now, it is used as a standard tool to determine blood sugar control in patients known to have diabetes. [20]

What are the acute complications of diabetes?

1. Severely elevated blood sugar levels due to an actual lack of insulin or a relative deficiency of insulin. [21]
2. Abnormally low blood sugar levels due to too much insulin or other glucose-lowering medications. [22]
3. Insulin is vital to patients with type 1 diabetes - they cannot live with out a source of exogenous insulin. Without insulin, patients with type 1 diabetes develop severely elevated blood sugar levels. This leads to increased urine glucose, which in turn leads to excessive loss of fluid and electrolytes in the urine. Lack of insulin also causes the inability to store fat and protein along with breakdown of existing fat and protein stores. This dysregulation, results in the process of ketosis and the release of ketones into the blood. Ketones turn the blood acidic, a condition called diabetic ketoacidosis(DKA). Symptoms of diabetic ketoacidosis include nausea, vomiting, and abdominal pain. [23]
4. Diabetic ketoacidosis can be caused by infections, stress, or trauma all which may increase insulin requirements. In addition, missing doses of insulin is also an obvious risk factor for developing diabetic ketoacidosis. Urgent treatment of diabetic ketoacidosis involves the intravenous administration of fluid, electrolytes, and insulin, usually in a hospital intensive care unit. Dehydration can be very severe, and it is not unusual to need to replace 6-7 liters of fluid when a person presents in diabetic ketoacidosis. Antibiotics are given for infections. [24]
5. Hypoglycemia means abnormally low blood sugar (glucose). In patients with diabetes, the most common cause of low blood sugar is excessive use of insulin or other glucoselowering medications, to lower the blood sugar level in diabetic patients in the presence of a delayed or absent meal. When low blood sugar levels occur because of too much insulin, it is called an insulin reaction. [25]
6. Sometimes, low blood sugar can be the result of an insufficient caloric intake or sudden excessive physical exertion.[26]

What are the chronic complications of diabetes?

These diabetes complications are related to blood vessel diseases and are generally classified into small vessel disease, such as those involving the eyes, kidneys and nerves (microvascular disease), and large vessel disease involving the heart and blood vessels (macrovascular disease). Diabetes accelerates hardening of the arteries (atherosclerosis) of the larger blood vessels, leading to coronary heart disease (angina or heart attack), strokes, and pain in the lower extremities because of lack of blood supply (claudication).

For more information, please read the following articles: Stroke, and Heart Attack.[27]

Eye Complications

The major eye complication of diabetes is called diabetic retinopathy. Diabetic retinopathy occurs in patients who have had diabetes for at least 5 years. Diseased small blood vessels in the back of the eye cause the leakage of protein and blood in the retina.

Disease in these blood vessels also causes the formation of small aneurysms (microaneurysms), and new but brittle blood vessels (neovascularization). Spontaneous bleeding from the new and brittle blood vessels can lead to retinal scarring and retinal detachment, thus impairing vision.[28]

Kidney damage Kidney damage from diabetes is called diabetic nephropathy. The onset of kidney disease and its progression is extremely variable. Initially, diseased small blood vessels in the kidneys cause the leakage of protein in the urine. Later on, the kidneys lose their ability to cleanse and filter blood. The accumulation of toxic waste products in the blood leads to the need for dialysis. Dialysis involves using a machine that serves the function of the kidney by filtering and cleaning the blood. In patients who do not want to undergo chronic dialysis, kidney transplantation can be considered. [29]

Nerve damage Nerve damage in diabetes is called diabetic neuropathy and is also caused by disease of small blood vessels. In essence, the blood flow to the nerves is limited, leaving the nerves without blood flow, and they get damaged or die as a result (a term known as ischemia). Symptoms of diabetic nerve damage include numbness, burning, and aching of the feet and lower extremities. Shoes or other protection should be worn as much as possible. Seemingly minor skin injuries should be attended to promptly to avoid serious infections. Because of poor blood circulation, diabetic foot injuries may not heal. Sometimes, minor foot injuries can lead to serious infection, ulcers, and even gangrene, necessitating surgical amputation of toes, feet, and other infected parts. [30]

Diabetic nerve damage can affect the nerves that are important for penile erection, causing erectile dysfunction (ED, impotence). Erectile dysfunction can also be caused by poor blood flow to the penis from diabetic blood vessel disease. Diabetic neuropathy can also affect nerves to the stomach and intestines, causing nausea, weight loss, diarrhea, and other symptoms of gastroparesis(delayed emptying of food contents from the stomach into the intestines, due to ineffective contraction of the stomach muscles). [31]

The pain of diabetic nerve damage may respond to treatment with gabapentin (Neurontin), phenytoin (Dilantin), carbamazepine (Tegretol), desipramine (Norpramin ine), amitriptyline (Elavil), or with topically-applied capsaicin (an extract of pepper). Neurontin, Dilantin and Tegretol are medications that are traditionally used in the treatment of seizure disorders.

Elavil and Norpraminine are medications that are traditionally used for depression. The pain of diabetic nerve damage may also improve with better blood sugar control. New medications for nerve pain are being studied [32]

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What can be done to slow diabetes complications?

Findings from the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) have clearly shown that aggressive and intensive control of Elevated levels of blood sugar in patients with type 1 and type 2 diabetes decreases the complications Of nephropathy, neuropathy, retinopathy, and may reduce the occurrence and severity of large blood Vessel diseases. Aggressive control with intensive therapy means achieving fasting glucose levels Between 70 -120 mg/dl; glucose levels of less than 180 mg/dl after meals; and a near normal hemoglobin A1C levels.[34]

• How is diabetes treated?

The major goal in treating diabetes is controlling elevated blood sugars (glucose) without causing Abnormally low levels of blood sugar. Type 1 diabetes is treated with insulin, exercise, and a diabetic diet. Type 2 diabetes is first treated with weight reduction, a diabetic diet, and exercise.

Weight reduction and exercise are important treatments of diabetes. Weight reduction and exercise Increase the body's sensitivity to insulin, thus helping to control blood sugar elevations. For more,please read the Weight Loss and Fitness articles.[35]

Medications for type 2 diabetes

All the information listed below applies to patients who are not pregnant or breastfeeding. At present The only recommended way of controlling diabetes in these situations is by diet, exercise and insulin Therapy. You should refer to your doctor if you are on these medications and are considering becoming pregnant, or if you have become pregnant while taking these medications. Based on what is known, medications for type 2 diabetes are designed to:

1.Increase the insulin output by the pancreas.

2. Decrease the amount of glucose released from the liver.

3. Increase the sensitivity (response) of cells to insulin.

4. Decrease the absorption of carbohydrates from the intestine.

5. Slow gastric emptying to delay the presentation of carbohydrates for absorption in the small intestine.

Patients with diabetes should never forget the importance of diet and exercise. The control of ?Diabetes starts with a healthy lifestyle regardless of what medications are being used.

• Medications that increase the insulin output by the pancreas – sulfonylureas and meglitinides

Sulfonylureas

Historically, increasing the insulin output by the pancreas has been the major area targeted by medications used to treat type 2 diabetes. These medications belong to a class of drugs called sulfonylureas. Sulfonylureas primarily lower blood glucose levels by increasing the release of .[37] insulin from the pancreas. Older generations of these drugs include chlorpropamide and tolbutamide, while newer drugs include glyburide (DiaBeta), glipizide (Glucotrol), and glimepiride (Amaryl). These drugs are effective in rapidly lowering blood sugars, but run the risk of causing hypoglycemia Meglitinides.[36]

- repaglinide (Prandin) and nateglinide (Starlix) Recently, a new class of drugs that affect insulin release has been approved by the FDA for use in type 2 diabetes. This class is known as meglitinides and these drugs also work on the pancreas to promote insulin secretion. Unlike sulfonylureas that bind to receptors on the insulin producing cells, meglitinides work through a separate potassium based channel on the cell surface[37]

Prandin

In a 3-month study, repaglinide (Prandin) dropped fasting blood glucose values by 61 mg/dL and post meal blood glucose values by 100 mg/dL. Because Prandin is short acting and given before meals, it is particularly beneficial in lowering blood glucose after meals and does not tend to lower fasting glucose levels to the same degree. Prandin has been used in combination with other medications, such as metformin (Glucophage), with impressive results. In 83 patients with type 2 diabetes, blood sugar control improved significantly with the addition of Prandin to Glucophage. Prandin does interact with other medications. The doctor must be aware of all other medications the patient is taking before prescribing Prandin. The usual starting dose is 0.5mg before each meal, and can be increased to 4 mg. The maximum daily dose is 16 mg.[38]

Starlix

Nateglinide (Starlix) has essentially the same profile of side effects and interactions as Prandin. The major benefit of Starlix is that the starting dose of 120mg does not need to be adjusted upward, but rather remains constant. These medications are also relatively safe to use in people with impaired kidney function. For more, please read the drug information pamphlet on nateglinide.[39]

Medications that decrease the amount of glucose produced by the live

r A class of drugs called biguanides has been used for many years in Europe and Canada. In 1994, the FDA approved the use of metformin (Glucophage) for the treatment of type 2 diabetes in the United States. Glucophage is unique in its ability to decrease glucose production from the liver. Briefly, because metformin does not increase insulin levels, when used alone, In addition, metformin has an effect whereby it tends to suppress appetite, which may be beneficial in this population. Metformin may be used by itself or in conjunction with other oral agents, or insulin. It should not be used in patients with kidney impairment, and should be used with caution in those with liver impairment. The older parent compounds of metformin were associated with a serious condition called lactic acidosis with a dangerous acid build up in the blood resulting from accumulation of the drug and its breakdown products. While metformin is safer in this regard, it is recommended that the drug be discontinued for 24 hours before any dye-related procedure (such as IVP kidney study) or surgery is performed. The dyes may impair kidney function and cause a build up of the drug in the blood. Metformin

can be restarted after these procedures once the patient has urinated normally.[40]

Medications that increase the sensitivity of cells to insulin

At present in the United States, the class of drugs known as thiazolidinediones lowers blood glucose by improving target cell response to insulin (increasing the sensitivity of the cells to insulin). Troglitazone (Rezulin) was the first of this type of compound introduced in the United States. Because of severe toxic liver effects, troglitazone has been taken off the market. Sister compounds are now available with a better safety profile.[[41]

These drugs include pioglitazone (Actos) and rosiglitazone (Avandia).

Pioglitazone (Actos) and rosiglitazone (Avandia) are new thiazolidinediones that have been approved for use in the United States. While they are sister compounds to Rezulin, extensive studies have failed to show any liver problems associated with these particular drugs. Patients should be aware, however, that these drugs are still relatively new, and its long-term safety profile is not yet known. Both Avandia and Actos act by increasing the sensitivity (responsiveness) of cells to insulin. It improves sensitivity to insulin in muscle and fat tissue. These drugs have been effective in lowering blood sugars in patients with type 2 diabetes, Actos and Avandia act within 1 hour of administration and are dosed daily. It is important to note that it takes up to 6 weeks to see a drop in blood glucose levels on these agents and up to 12 weeks to see a maximum benefit. Actos and Avandia have been approved as first line therapy in diabetes, and for use in combination. Both medications may be used in patients taking other oral agents as well as those using insulin.[42]

Medications that decrease the absorption of carbohydrates from the intestine

Before being absorbed into the bloodstream, carbohydrates must be broken down into smaller sugar particles, such as glucose, by enzymes in the small intestine. One of the enzymes involved in breaking down carbohydrates is called alpha glucosidase. By inhibiting this enzyme, carbohydrates are not broken down as efficiently and glucose absorption is delayed.[43]

Precose

The name of the alpha glucosidase inhibitor available in the United States is Precose. In clinical trials with over 700 patients, the use of acarbose (Precose) showed a reduction in hemoglobin A1c values (a well known measurement of 3 month average blood sugars) significantly greater than the placebo (no treatment). However, as a single agent, Precose is not as effective as the other medications listed. Since Precose works on the intestine, its effects are additive to diabetic medications that work at other sites, such as sulfonylureas. Clinical studies have shown statistically better blood glucose control in patients treated with Precose and a sulfonylurea versus the sulfonylurea alone. Precose is currently used alone or in combination with a sulfonylurea[44]

• New medications that effect glycemic control

Symlin (pramlintide)

Symlin is the first in a new class of injected antihyperglycemic medications for use in patients with type 2 or type 1 diabetes treated with insulin. Pramlintide, the active ingredient in Symlin, is a synthetic analog of human amylin, a naturally occurring neuroendocrine hormone synthesized from pancreatic beta cells that contributes to glucose control during the postprandial period. Amylin, similar to insulin, is absent or deficient in patients with diabetes. When used with insulin, this compound can help patients achieve improved glycemic control with additional benefits that cannot be realized with insulin alone.[45]

Symlin is taken just prior to meals, three times a day. It is given in injection form and is indicated for:

• Type 2 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and have failed to achieve desired glucose control despite optimal insulin therapy, with or without a concurrent sulfonylurea agent and/or metformin.

• Type 1 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy. Symlin is considered a therapy option in patients with insulin-using type 2 or type 1 diabetes who are unable to achieve adequate glycemic control despite individualized insulin management. Insulin-using patients with type 2 diabetes may also be taking a concurrent sulfonylurea agent and/or metformin.[46]

Byetta (exenatide)

Byetta (exenatide) is a new medication on the market that has it's origins in an interesting place--the Gila monster's saliva. Scientists studying this small lizard noted it could go a long time without eating. They

found a substance in it's saliva that slowed stomach emptying, thus making the lizard feel fuller longer.

This substance was similar in nature to a gut hormone found in humans known as GLP-1. Thus, the studies began. Ultimately, after modifying this hormone, exenatide (with the trade name Byetta) was developed. Byetta is the first in a new class of drugs for the treatment of type 2 diabetes called incretin mimetics. Byetta has been shown to have many of the same effects on sugar regulation as GLP-1, so it mimics the body's natural physiology for self-regulating blood sugar. [47]

Combination Medications

Glyburide/metformin (Glucovance),
rosiglitazone/metformin (Avandamet),
glipizide/metformin (Metaglip)

3 relatively new combination pills that are on the market to treat diabetes. Glucovance combines glyburide with metformin in varying doses. Avandamet is a combination of varying doses of Avandia and metformin. And Metaglip is a combination pill containing glipizide and metformin in varying strengths. The benefit to these agents is fewer pills to take, hopefully leading to better compliance. While they work well, I personally like to give patients individual medications, until I know what doses are working, and then switch to a combination pill once the patient has been stable on the doses of individual medications for a period of time.[48]

 Treatment of diabetes with insulin

Insulin is the mainstay of treatment for patients with type 1 diabetes. Insulin is also important in type 2 diabetes when blood glucose levels cannot be controlled by diet, weight loss, exercise, and oral medications2 .

Ideally, insulin medication should be administered in a manner that mimics the natural pattern of insulin secretion by a healthy pancreas. The complex pattern of insulin secretion by the pancreas is difficult to duplicate. Still, adequate blood glucose control can be achieved with careful attention to diet, regular exercise, home blood glucose monitoring, and multiple insulin injections throughout the day. For more, please see the Diabetes and Home Care Monitoringarticle.[49]

For example, a patient may take an injection of Lente in the morning and evening to provide a baseline of insulin throughout a 24-hour period. In addition, the same patient may take an injection of Humalog just before meals to cover the increase in carbohydrate load after eating.

Different methods of delivering insulin

Not only is the variety of insulin preparations available growing, so are the methods for administering insulin.[50]

Pre-filled insulin pens

In the past, insulin was available only in an injectable form. This involved carrying syringes (which a few decades ago were made of glass and required sterilization), needles, vials of insulin, and alcohol swabs. Needless to say, patients often found it difficult to take multiple shots a day, and as a result, good blood sugar control was often compromised. Many pharmaceutical companies are now offering discreet and convenient methods of insulin delivery. Both Novo Nordisk and Lily have an insulin pen delivery system. This system is similar to an ink cartridge in a fountain pen. A small pen-sized device holds an insulin cartridge (usually containing 300 units). Cartridges are available in the most widely used insulin formulations, such as those listed in the table above. The amount of insulin to be injected is dialed in by turning the bottom of the pen until the required number of units is seen in the dose-viewing window. The tip of the pen consists of a needle that is replaced with each injection. A release mechanism allows the needle to penetrate just under the skin and deliver the required amount of insulin. The cartridges andneedles are disposed of when finished and new ones are simply inserted. In many cases the entire pen is disposed of. These insulin delivery devices are discreet and less cumbersome than traditional methods.[51]

 Insulin pump

The most recently available advance in insulin delivery is the insulin pump. In the United States, MiniMed, Deltec and Disetronic market the insulin pump. An insulin pump is composed of a pump reservoir similar to that of an insulin cartridge, a battery-operated pump, and a computer chip that allows the user to control the exact amount of insulin being delivered. Currently, pumps on the market are about the size of a beeper. The pump is attached to a thin plastic tube (an infusion set) that has a soft cannula (or needle) at the end through which insulin passes. This cannula is inserted under the skin, usually on the abdomen. The cannula is changed every 2 days. The tubing can be disconnected from the pump while

showering or swimming. The pump is used for continuous insulin delivery, 24 hours a day. The amount of insulin is programmed and is administered at a constant rate (basal rate). Often, the amount of insulin needed over the course of 24 hours varies depending on factors like exercise, activity level, and sleep.[52]

 Inhalation

Another promising route of insulin administration is through inhalation. Inhaled insulin is currently being tested but has not been approved by the United States Food and Drug Administration (FDA). Many devices are available that allow for other medications to be used in this manner, the best example of which is asthma therapy. Insulin is not absorbed through the bronchial tubes (airways), and must reach the air sacks at the end of the bronchial tubes to be absorbed. Once at the alveoli, insulin can be absorbed and enter the bloodstream. Currently, powdered inhalers and nebulizers are being studied to determine which delivery system is the most reliable. The safety of inhaled insulin still needs to be established before a product for consumer use can be made available. Trials are currently underway to establish the safety of inhaled insulin. These trials are well into phase III, meaning that human subjects have already used inhaled insulin and the results are promising. Inhaled insulin will likely be on the market within the next 1-2 years.[53]

Intranasal, Transdermal, PILL

Other routes for the delivery of insulin have also been tried. Intranasal insulin delivery was thought to be promising. However, this method was associated with poor absorption and nasal irritation. Transdermal insulin (skin patch delivery) has also yielded disappointing results to date. Insulin in pill form is also not yet effective since the digestive enzymes in the gut break it down.[54]

II. CONCLUSION

• Diabetes is a chronic condition associated with abnormally high levels of sugar (glucose) in the blood.
• Insulin produced by the pancreas lowers blood glucose. • Absence or insufficient production of insulin causes diabetes.
• The two types of diabetes are referred to as type 1 (insulin dependent) and type 2 (non-insulin dependent).
• Symptoms of diabetes include increased urine output, thirst and hunger as well as fatigue.
• Diabetes is diagnosed by blood sugar (glucose) testing. • The major complications of diabetes are both acute and chronic.
• Acutely: dangerously elevated blood sugar, abnormally low blood sugar due to diabetes medications may occur Chronically: disease of the blood vessels (both small and large) which can damage the eye, kidneys, nerves, and heart may occur
• Diabetes treatment depends on the type and severity of the diabetes. Type 1 diabetes is treated with insulin, exercise, and a diabetic diet. Type 2 diabetes is first treated with **r** weight reduction, a diabetic diet, and exercise. When these measures fail to control the elevated blood sugars, oral medications are used. If oral medications are still insufficient, insulin medications are

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