

Brief Review on Diabetes – A Metabolic Disease

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INTRODUCTION

Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced.^[10] There are three main types of diabetes mellitus: Type 1 DM results from the pancreas' failure to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown. Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is a combination of excessive body weight and insufficient exercise. Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels. Prevention and treatment involve maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Control of blood pressure and maintaining proper foot care are important for people with the disease. Type 1 DM must be managed with insulin injections. Type 2 DM may be treated with medications with or without insulin. Insulin and some oral medications can cause low blood sugar. Weight loss surgery in those

with obesity is sometimes an effective measure in those with type 2 DM. Gestational diabetes usually resolves after the birth of the baby.

DIABETES SYMPTOMS

The following symptoms of diabetes are typical. However, some people with type 2 diabetes have symptoms so mild that they go unnoticed.

COMMON SYMPTOMS OF DIABETES

- Urinating often
- Feeling very thirsty
- Feeling very hungry - even though you are eating
- Extreme fatigue
- Blurry vision
- Cuts/bruises that are slow to heal
- Weight loss - even though you are eating more (type 1)
- Tingling, pain, or numbness in the hands/feet (type 2)

Early detection and treatment of diabetes can decrease the risk of developing the complications of diabetes. Although there are many similarities between type 1 and type 2 diabetes, the cause of each is very different. And the treatment is usually quite different, too. Some people, especially adults who are newly diagnosed with type 1 diabetes, may have symptoms similar to type 2 diabetes and this overlap between types can be confusing.

DIAGNOSING DIABETES AND LEARNING ABOUT PREDIABETES

There are several ways to diagnose diabetes. Each way usually needs to be repeated on a second day to diagnose diabetes. Testing should be carried out in a health care setting (such as your doctor's

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office or a lab). If your doctor determines that your blood glucose level is very high, or if you have classic symptoms of high blood glucose in addition to one positive test, your doctor may not require a second test to diagnose diabetes.

A1C- The A1C test measures your average blood glucose for the past 2 to 3 months. The advantages of being diagnosed this way are that you don't have to fast or drink anything.

Diabetes is diagnosed at an A1C of greater than or equal to 6.5%

Result	A1C
Normal	less than 5.7%
Prediabetes	5.7% to 6.4%
Diabetes	6.5% or higher

Fasting Plasma Glucose (FPG)- This test checks your fasting blood glucose levels. Fasting means after not having anything to eat or drink (except water) for at least 8 hours before the test. This test is usually done first thing in the morning, before breakfast. Diabetes is diagnosed at fasting blood glucose of greater than or equal to 126 mg/dl

Result	Fasting Plasma Glucose (FPG)
Normal	less than 100 mg/dl
Prediabetes	100 mg/dl to 125 mg/dl
Diabetes	126 mg/dl or higher

Oral Glucose Tolerance Test (also called the OGTT)-

The OGTT is a two-hour test that checks your blood glucose levels before and 2 hours after you drink a special sweet drink. It tells the doctor how your body processes glucose. Diabetes is diagnosed at 2 hour blood glucose of greater than or equal to 200 mg/dl

Result	Oral Glucose Tolerance Test (OGTT)
Normal	less than 140 mg/dl
Prediabetes	140 mg/dl to 199 mg/dl
Diabetes	200 mg/dl or higher

Random (also called Casual) Plasma Glucose Test-

This test is a blood check at any time of the day when you have severe diabetes symptoms. Diabetes is diagnosed at blood glucose of greater than or equal to 200 mg/dl

Some people with prediabetes may have some of the symptoms of diabetes or even problems from diabetes already. You usually find out that you have prediabetes when being tested for diabetes.

If you have prediabetes, you should be checked for type 2 diabetes every one to two years.

Results indicating prediabetes are:

An A1C of 5.7% – 6.4%

Fasting blood glucose of 100 – 125 mg/dl

An OGTT 2 hour blood glucose of 140 mg/dl – 199 mg/dl

TYPE OF DIABETES

Type-1 Diabetes

Millions of people around the world live with diabetes or know someone living with diabetes. The majority have type 2 diabetes, but an important minority have type 1 diabetes (~5%). Contrary to popular belief, type 1 diabetes is not a childhood disease. It occurs at every age, in people of every race, and of every shape and size. In fact, there are more adults who have type 1 diabetes than children, although it was previously known as juvenile diabetes. In type 1 diabetes, the body does not produce insulin. The body breaks down the carbohydrates you eat into blood glucose (also called blood sugar), which it uses for energy. Insulin is a hormone that the body needs to get glucose from the bloodstream into the cells of the body. With the help of insulin therapy and other treatments, even young children can learn to manage their condition and live long, healthy lives.

Type-2 Diabetes

Diabetes is a problem with your body that causes blood glucose (sugar) levels to rise higher than normal. This is also called hyperglycemia. Type 2 diabetes is the most common form of diabetes. If you have type 2 diabetes your body does not use insulin properly. This is called insulin resistance. At first, your pancreas makes extra insulin to make up for it. But, over time it isn't able to keep up and can't make enough insulin to keep your blood glucose at normal levels.

Gestational Diabetes

During pregnancy – usually around the 24th week – many women develop gestational diabetes. A diagnosis of gestational diabetes doesn't mean that you had diabetes before you conceived, or that you will have diabetes after giving birth. But it's important to follow your doctor's advice regarding blood glucose (blood sugar) levels while you're planning your pregnancy, so you and your baby both remain healthy.

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Type 1.5 Diabetes

Type- 1.5 diabetes is a non-official term that is sometimes used to refer to a form of type 1 diabetes known as Latent Autoimmune Diabetes in Adults (LADA). The term type 1.5 refers to the fact that the condition is a form of type 1 diabetes that can share some features that are more commonly associated with type 2 diabetes. Type 1.5 diabetes is diagnosed during adulthood as are most cases of type 2 diabetes. Type 1.5 diabetes also has a slow onset, similar to type 2 diabetes. However, type 1.5 diabetes is an autoimmune disease like type 1 diabetes and will almost certainly require insulin therapy at some point in the future.

Type 3 Diabetes

Type-3 diabetes is a title that has been proposed for Alzheimer’s disease which results from resistance to insulin in the brain. Studies carried out by the research team at Warren Alpert Medical School at Brown University identified the possibility of a new form of diabetes after finding that insulin resistance can occur in the brain. The researchers pinpoint resistance to insulin and insulin-like growth factor as being a key part of the progression of Alzheimer’s disease. Whereas type 1 and type 2 diabetes are

characterised by hyperglycemia (increased blood sugar), a separate study, carried out by the University of Pennsylvania and published in 2012, excluded people with a history of diabetes, indicating that Alzheimer’s can develop without the presence of significant hyperglycemia in the brain.

ORAL DIABETIC MEDICINES AVAILABLE IN MARKET

Type 2 diabetes results when the body is unable to produce the amount of insulin it needs to convert food into energy or when it is unable to use insulin appropriately. Sometimes the body is actually producing more insulin than is needed by a person to keep blood glucose in a normal range. Yet blood glucose remains high, because the body’s cells are resistant to the effects of insulin. Physicians and scientists believe that type 2 diabetes is caused by many factors, including insufficient insulin and insulin resistance. They increasingly believe that the relative contribution each factor makes toward causing diabetes varies from person to person. It is important to know the name of your diabetes medicine (or medicines), how it is taken, the reasons for taking it and possible side-effects.

Diabetes Pills	How to Take	How They Work	Side Effects	Of Note
Biguanides Metformin (Glucophage) Metformin liquid (Riomet) Metformin extended release (Glucophage XR, Fortamet, Glumetza)	Metformin: usually taken twice a day with breakfast and evening meal. Metformin extended release: usually taken once a day in the morning.	Decreases amount of glucose released from liver.	Bloating, gas, diarrhea, upset stomach, loss of appetite (usually within the first few weeks of starting). Take with food to minimize symptoms. Metformin is not likely to cause low blood glucose. In rare cases, lactic acidosis may occur in people with abnormal kidney or liver function.	Always tell healthcare providers that it may need to be stopped when you are having a dye study or surgical procedure.
Sulfonylureas Glimpiride (Amaryl) Glyburide (Diabeta, Micronase) Glipizide (Glucotrol, Glucotrol XL) Micronized glyburide (Glynase)	Take with a meal once or twice a day.	Stimulates the pancreas to release more insulin, both right after a meal and then over several hours	Low blood glucose, occasional skin rash, irritability, upset stomach	Because these medicines can cause low blood glucose, always carry a source of carbohydrate with you. Follow your meal plan and activity program. Call your healthcare provider if your blood glucose levels are consistently low. If there is an increase in your activity level or reduction in your weight or calorie intake, the dose may need to be lowered.

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Meglitinides Repaglinide (Prandin) D-Phenylalanine Derivatives Nateglinide (Starlix)	Both of these medications should be taken with meals. If you skip a meal, skip the dose.	Stimulate the pancreas to release more insulin right after a meal.	Effects diminish quickly and they must be taken with each meal; may cause low blood glucose.	These work quickly when taken with meals to reduce high blood glucose levels. However, they are less likely than sulfonylureas to cause low blood glucose.
Thiazolidinediones Pioglitazone (TZDs) Pioglitazone (Actos)	Usually taken once a day; take at the same time each day.	Makes the body more sensitive to the effects of insulin.	May cause side effects such as swelling (edema) or fluid retention. Do not cause low blood sugar when used alone. Increased risk of congestive heart failure in those at risk.	Increases the amount of glucose taken up by muscle cells and keeps the liver from overproducing glucose; may improve blood fat levels. Talk with your healthcare provider if you have the following symptoms: nausea, vomiting, fatigue, loss of appetite, shortness of breath, severe edema or dark urine.
DPP-4 Inhibitors Sitagliptin (Januvia) Saxagliptin (Onglyza) Linagliptin (Tradjenta)	Take once a day at the same time each day.	Improves insulin level after a meal and lowers the amount of glucose made by your body.	Stomach discomfort, diarrhea, sore throat, stuffy nose, upper respiratory infection. Do not cause low blood glucose.	Can be taken alone or with metformin, a sulfonylurea or Actos. Tell your healthcare provider if you have any side effects that bother you or that don't go away .
Alpha-glucosidase Inhibitors Acarbose (Precose) Miglitol (Glyset)	Take with first bite of the meal; if not eating, do not take.	Slows the absorption of carbohydrate into your bloodstream after eating.	Gas, diarrhea, upset stomach, abdominal pain	Take with meals, to limit the rise of blood glucose that can occur after meals; these do not cause low blood glucose. Side effects should go away after a few weeks. If not, call your healthcare provider.
Bile Acid Sequestrants Colesevelam (Welchol)	Take once or twice a day with a meal and liquid.	Works with other diabetes medications to lower blood glucose.	Constipation, nausea, diarrhea, gas, heartburn, headache (may interact with glyburide, levothyroxine and contraceptives)	Primary effect, when used either alone or with a statin, is to lower LDL cholesterol; has blood glucose-lowering effect when taken in combination with certain diabetes medications. Before taking this medication, tell your healthcare provider if you have high triglycerides (blood fats) or stomach problems. If you take thyroid medication or glyburide, take them 4 hours before taking Welchol. Tell your healthcare provider if you have side effects that bother you or that don't go away .

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Combination Pills Pioglitazone & metformin (Actoplus Met) Glyburide & metformin (Glucovance) Glipizide & metformin (Metaglip)	Check with your provider; usually taken once a day.	Combines the actions of each pill used in the combination.	Side effects are the same as those of each pill used in the combination. Some combination pills may lead to low blood glucose levels if one of the medications contained in the combination has this effect.	May decrease the number of pills you need to take.
Sitagliptin & metformin (Janumet) Saxagliptin & metformin (kombiglyze) Repaglinide & metformin (Prandin) Pioglitazone & glimepiride (Duetact)				

CONCLUSION

Diabetes is an alarming disorder of the third world. The prevalence of diabetes is likely to increase by 35% by the year 2025 according to the World Health Organization (WHO) projections. Currently, India is the diabetic capital of the world. Diabetes mellitus, a group of metabolic diseases is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Diabetes mellitus is generally categorized as type 1 (insulin dependant diabetes or juvenile-onset diabetes), type 2 (non-insulin dependent or adult onset diabetes) and gestational diabetes. Type 1 results due to autoimmunity and type 2 because of insulin resistance. There is yet another form of diabetes which phenotypically resembles type 2, but genotypically resembles type 1. This form of diabetes is known as type 1.5 diabetes or latent autoimmune diabetes (LADA). Type 1.5 diabetes is often misdiagnosed as type 2 diabetes and hence, treatment for type 1.5 diabetes is similar to type 2 diabetes. As the pathophysiology of different types of diabetes varies, interventions for treating them should also be specific to its type. This essentially the need for correct categorization of diabetes.

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