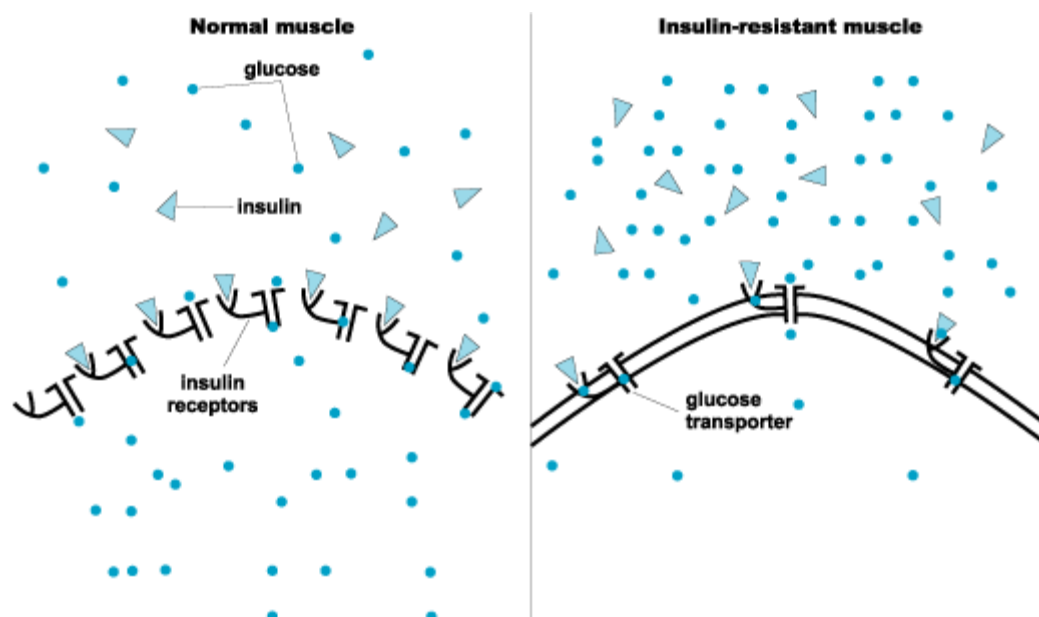


RESEARCH UPDATE

Type 2 diabetes

Diabetes mellitus is a disorder characterized by the presence of excess glucose in the blood and tissues of the body. The word "diabetes" comes from the Greek for "a siphon," referring to the discharge of an excess quantity of urine; the word "mellitus" comes from Latin for "honey." Thus, diabetes mellitus refers to the passage of large amounts of sweet urine. Diabetes is a disease in which the pancreatic hormone insulin is either not produced or not properly used by the body. It is characterized as a chronic metabolic disorder with hyperglycemia (high blood sugar) and abnormal energy metabolism. Diabetes is caused by a combination of genetic, autoimmune, and environmental factors.

A normal muscle cell may have as many as 20,000 insulin receptors. Insulin binds to the receptor and glucose can enter the cell: an insulin-resistant muscle may have as few as 5000 insulin receptors. This keeps blood sugars high and muscle glucose low.



There are two main types of diabetes: type 1 (insulin-dependent diabetes) and type 2 (non-insulin-dependent diabetes). Type 1 diabetes affects 5–10% of all people diagnosed with this disease. This type of diabetes is caused by the immune system's destruction of the β cells of the pancreas.

Of all the people who have diabetes, 90–95% have type 2 diabetes. In the past, type 2 diabetes was also termed adult onset diabetes because of its late onset (usually occurring after age 40). However, the term "adult onset" is no longer appropriate as there is a startling increase of type 2 diabetes in children as young as 10 years.

Clinically, a person may have type 2 diabetes for many years without being aware of it. Loss of vision, which usually takes years to develop, may be the first sign of the disease. The risks for developing type 2 diabetes include family history of type 2 diabetes, obesity, high blood pressure, high levels of cholesterol, a sedentary lifestyle, as well as development of diabetes during pregnancy (gestational diabetes). The causes of this disease are multifold. In type 2 diabetes, a defect in insulin action (insulin resistance) is combined with a defect in insulin secretion, which leads to hyperglycemia. Impaired insulin action has been demonstrated in

muscle, fat, and liver tissues. Although there is some evidence for a genetic link in the development of type 2 diabetes, it is increasingly clear that insulin resistance is an acquired defect in most cases of type 2 diabetes.

Obesity

Obesity is the most common cause of insulin resistance and type 2 diabetes. Simply being overweight (BMI > 25, where body mass index [BMI] is a measure used to evaluate body weight relative to height) raises the risk of developing type 2 diabetes by a factor of 3.

The location of body fat can significantly affect one's risk for developing diabetes. Doctors have long recognized that people who are apple-shaped—with their fat concentrated in the abdomen—are at much higher risk for diabetes and metabolic syndrome than those whose fat is mainly subcutaneous, that is, distributed beneath the skin primarily in the buttocks and thighs. In view of this finding, more physicians are suggesting that the waist-to-hip ratio is a more accurate measure of obesity and a better predictor of insulin resistance and metabolic syndrome than the widely used body mass index.

Diagnosis

The diagnosis of type 2 diabetes is made by using any of the following criteria: a random blood glucose level greater than 11.1 mmol/L (200 mg/dL); a fasting (8-hour) blood glucose level greater than 7 mmol/L (126 mg/dL); blood glucose levels greater than 11.1 mmol/L (200 mg/dL), measured 2 h after an oral glucose tolerance test (the ingestion of 75 g of glucose following an overnight fast).

Treatment

There are two main forms of treatment of type 2 diabetes: alterations in diet and physical activity, and oral hypoglycemic agents (drugs that lower blood glucose). There are four types of agents, with different modes of action.

1. The sulfonylurea types (for example, glibenclamide) stimulate the pancreas to produce more insulin, which may increase the amount of insulin binding to insulin receptors, allowing for greater glucose uptake into cells.
2. Alpha glucosidase inhibitors inhibit the digestion of carbohydrates in food and hence reduce their absorption in the gut. An example is Acarbose, which slows the absorption of carbohydrate foods. This can help prevent rises in blood glucose levels and is most often used in combination with other medications.
3. Orlistat blocks absorption of about 30% of the fat that is eaten. This does not specifically treat the diabetes but may help diabetes management in people having major problems achieving weight control.
4. The biguanide types (for example, Metformin) and the thiazolidinediones (that is, Troglitazone) reduce insulin resistance and result in greater uptake of glucose by tissues. These aim to overcome the major problem of insulin resistance in type 2 diabetes. This class of medication (usually Metformin) is often the first choice for overweight teenagers with type 2 diabetes and can be very effective in combination with healthy lifestyle measures.

Insulin resistance

Insulin resistance can be said to exist when a normal concentration of insulin elicits a subnormal biological response. Impaired insulin action in diabetes has been demonstrated in muscle, fat, and liver tissues.

Metabolic syndrome

The metabolic syndrome is a group of metabolic risk factors for cardiovascular disease. There are five cardiovascular risk factors that accompany the metabolic syndrome: (1) dyslipidemia [elevated apolipoprotein B (apo B), elevated triglyceride, small low-density lipoprotein (LDL) particles, and low levels of high-density lipoprotein (HDL) cholesterol]; (2) elevated blood pressure; (3) elevated glucose; (4) a

prothrombotic state; (5) a proinflammatory state.

The likelihood of an individual developing metabolic syndrome is enhanced by underlying risk factors, including obesity, insulin resistance, lack of physical activity, and advancing age. Besides being at higher risk for cardiovascular disease, people with metabolic syndrome are at increased risk for type 2 diabetes. The two major therapeutic strategies for treatment of affected persons are modification of the underlying risk factors and separate drug treatment of the particular metabolic risk factors when appropriate. First-line therapy for underlying risk factors is lifestyle changes, that is, weight loss in obese persons, increased physical activity, and diet modification. These changes will improve all of the metabolic risk factors. Whether use of drugs to reduce insulin resistance is effective, safe, and cost-effective before the onset of diabetes awaits the results of more clinical research. Individual risk components can be addressed with different treatments, such as antihypertensive therapies and statins for lowering blood lipids.

To be considered to have metabolic syndrome, a person must have insulin resistance plus two or more of the following: central obesity [waist circumference >102 cm (40 in.) (male) or >88 cm (35 in.) (female)]; dyslipidemia (triglycerides >2.0 mmol/L (36 mg/dL) or HDL cholesterol <1.0 mmol/L (<18 mg/dL)]; hypertension (blood pressure greater than 140/90 mmHg); hyperglycemia (fasting blood glucose >6.1 mmol/L, 110 mg/dL).

Exercise

Exercise is important for managing type 2 diabetes. Exercise has many benefits, including weight control, increasing glucose uptake by cells, helping insulin work better, as well as general fitness and health. It is important to do moderate exercise regularly (preferably every day or at least four times per week). Moderate exercise is an amount which makes you puff a bit, but you should still be able to carry on a conversation during the exercise. Aim for 30 to 45 minutes of moderate exercise at least four times per week.

Physical exercise helps the body utilize glucose by "sensitizing" the body to insulin. This means that for the same amount of insulin, more glucose can enter the muscle cells.

Since obesity is one of the main contributors to type 2 diabetes, as well as other diseases such as heart disease and stroke, exercising becomes an important tool to combat this. A recent national study in the United States (Diabetes Prevention Program) demonstrated that moderate exercise helped to prevent diabetes in people at high risk for type 2 diabetes.

Exercise also is beneficial as a prevention in that it lowers blood pressure (a risk factor for developing type 2 diabetes). Hypertension can lead to vascular problems in the diabetic, including blindness, kidney failure, and gangrene of the limbs.

Many people with type 1 and type 2 diabetes have high levels of cholesterol and/or triglycerides. These can lead to hardening of blood vessels. Exercise and good blood sugar control are the best ways to reduce blood triglyceride levels. Exercise may also help remove cholesterol from blood vessel walls by increasing HDL.

The only way humans can increase insulin sensitivity is by exercising. As a result of exercise, the person is more sensitive to insulin, the insulin can work more efficiently, and a lower daily dose of medication is usually required. Regular exercise (and weight loss) allows some people with type 2 diabetes to stop insulin injections and change to oral medication. It is now believed that many of the beneficial effects of exercise on the risk of heart disease, particularly in type 2 diabetes, are due to improvements with insulin sensitivity. It is thus important to exercise regularly and even vigorously.

See also: Carbohydrate metabolism; Diabetes; Glucose; Insulin; Obesity; Pancreas disorders

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Bibliography

- K. F. Petersen and G. I. Shulman, Etiology of insulin resistance, *Amer. J. Med.*, 119(5A):105–165, 2006

Additional Readings

- Related Web Site: Barbara Davis Center for Childhood Diabetes
- Related Web Site: Centers for Disease Control and Prevention
- Related Web Site: Joslin Diabetes Center

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