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Diagnosis of Diabetes is a Very Complex Procedure

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Abstract

Diabetes is a condition of chronic hyperglycemia, ie elevated blood sugar levels. The consequences of diabetes are multiple, starting from the occurrence of chronic vascular and non-vascular complications to a decrease in the quality, manner and length of life. There are several types of diabetes, but the most common is type 2. More than 90% of people with this disease have it, most often between the ages of 40 and 59, although the lower age limit is lower. This type of diabetes has a strictly genetic predisposition, but the influence of environmental factors is important. The immediate cause of the disease is a disorder of the pancreas which cannot produce enough of the hormone insulin necessary to supply the body's cells with energy from glucose. That is why it is extremely important to notice the symptoms of this disease early in order to successfully treat and mitigate the consequences. A person with diabetes may have the following symptoms: thirst and dry mouth, frequent urination, weight loss, increased hunger, fatigue and exhaustion, blurred vision, tingling in the feet, slow healing of wounds and infections. Type 1 diabetes usually develops suddenly, so the symptoms are more pronounced. Type 2 diabetes very often does not cause any unusual problems because it develops very gradually, so covert can last for years. Sometimes it is only discovered when complications of diabetes develop.

Keywords: Diabetes Type 1 and Type 2; Gestational Diabetes; Prediction.

Introduction

Thirst, tiredness, pruritus vulvae or balanitis, polyuria, and weight loss are the familiar symptoms of diabetes [1]. Patients do not, of course, always describe their symptoms in the clearest possible terms, or else their complaints may occur only as an indirect consequence of the more common features. Many patients describe dry mouth rather than thirst, and patients have been investigated for dysphagia when dehydration was the cause. Polyuria is often treated blindly with antibiotics; it may cause enuresis in young people and incontinence in elderly people and the true diagnosis is often overlooked. Complex urological investigations and even circumcision are sometimes performed before diabetes is considered.

The diagnosis of diabetes should no longer be missed. New patients attending their doctor, whether the family doctor, at a hospital outpatient clinic or accident and emergency department, should have a blood glucose measurement as a matter of routine, especially if their symptoms are unexplained. Only a few diabetic patients are wholly without symptoms and their diabetes should be detected by screening at any medical examination. Opportunistic screening for diabetes in this way is a duty.

There are three main types of diabetes. The most common are type 1 diabetes and type 2 diabetes [2]. A third type of diabetes, gestational diabetes, occurs during some pregnancies.

All types of diabetes result in too much sugar, or glucose, in the blood. To understand why this happens, it helps to understand how the body usually works. When you eat, your body breaks down your food into simpler forms such as glucose. The glucose goes into your bloodstream, where it travels to all the cells in your body. Your cells use glucose for energy. Insulin, a hormone made by the pancreas, helps move the glucose from the bloodstream to the cells.

The major goal for most patients with diabetes is to decrease A1C to <7% [3]. This has been shown consistently in many studies to decrease microvascular complications, including retinopathy, nephropathy, and neuropathy. If achieved soon after diagnosis, this goal has been associated with long-term reduction in macrovascular complications as well. Macrovascular complications include cardiovascular disease (CVD), stroke, and peripheral vascular disease. However, a more stringent goal of <6.5% is reasonable for selected patients, usually younger with a short duration of diabetes, long life expectancy, and no significant CVD. Hypoglycemia has been associated with an increased risk of death; thus, clinicians should be cognizant of hypoglycemia in certain populations. These are generally older patients with long-standing diabetes and/or a history of severe hypoglycemia, limited life expectancy, comorbidities, and advanced micro- or macrovascular complications. For these latter patients, a less stringent goal of A1C <8% would be reasonable. Patient attitude and expected treatment outcomes are also important determining factors for the approach to hyperglycemia management. Those who are high-

ly motivated, adherent, with excellent ability to perform self-care management and a good support system should be able to achieve more stringent goals.

Diabetic Neuropathies

Diabetic neuropathies (DN) are a heterogeneous group of disorders that include a wide range of abnormalities [4]. They can be focal or diffuse, proximal or distal, affecting both peripheral and autonomic nervous systems, causing morbidity with significant impact on the quality of life of the person with diabetes, resulting in early mortality. Distal symmetric polyneuropathy, the most common form of DN, usually involves small and large nerve fibers. Small nerve fiber neuropathy often presents with pain without objective signs or electrophysiologic evidence of nerve damage. However, there are now measures enabling early recognition of this type of neuropathy as a component of the impaired glucose tolerance and metabolic syndromes. The greatest risk of small fiber neuropathy is foot ulceration and subsequent gangrene and amputation. Large nerve fiber neuropathies produce numbness, ataxia and incoordination, impairing activities of daily living and causing falls and fractures. A careful history and detailed physical examination is essential for the diagnosis.

Symptomatic therapy has become available, and newer and better treatment modalities based on etiologic factors are being explored with potential for significant impact on morbidity and mortality. Preventive strategies and patient education still remain key factors in reducing complication rates and mortality. A number of mechanical measures for the treatment of neuropathy have been examined, and it is currently unclear whether or not these have salutary effects over and above those of placebo, and longer, well-controlled clinical trials are anticipated. In addition, there is the suggestion that surgical unentrapment of nerves in DN may confer symptomatic relief, but outside of clear applications in proven entrapments, this form of intervention has not been endorsed universally.

Gestational Diabetes

Gestational diabetes has an incidence of 14–25% in pregnancies complicated by obesity [5]. Maternal diabetes is associated with an increased incidence of fetal macrosomia, polycythaemia, intrauterine death, birth trauma and neonatal hypoglycaemia. In the medium term, the infant may have developmental delay. In the long term there may be metabolic complications for the offspring of the diabetic mother as adults in terms of obesity or early diabetes. The mothers have an increased risk of birth trauma due to the macrosomic infant and have an increased chance of developing type 2 diabetes in later life.

Gestational diabetes mellitus (GDM) can be defined as diabetes first discovered during pregnancy; it usually remits after pregnancy but this is not required to make the diagnosis. The increased incidence of GDM in obese pregnant women has been ascribed to increased insulin resistance combined with an insulin secretory deficit. Increasing BMI is associated with insulin insensitivity in normal pregnancy. As there is considerable evidence that GDM precedes type 2 diabetes these women probably represent a subset of insulin-resistant women who have inadequate insulin secretion in the face of insulin resistance. That being the case, the increased prevalence of obesity in women with GDM may represent a combined predisposition to both obesity and type 2 diabetes rather than obesity increasing the risk of type 2 diabetes per se.

Symptoms

Symptoms are similar in the two types of diabetes (Type 1 and Type 2), but they vary in their intensity [1]. The presentation is most typical and the symptoms develop most rapidly in patients with Type 1 diabetes; they usually develop over some weeks, but the duration may be a few days to a few months. There is usually considerable weight loss and exhaustion. If the diagnosis is missed, diabetic ketoacidosis occurs. Type 1 diabetes occurs under 40 years of age in approximately 70% of cases but can occur at any age, and even in older people.

Symptoms in patients with Type 2 diabetes are similar but tend to be insidious in their onset; sometimes these patients deny any symptoms, although they often admit to feeling more energetic after treatment has been started. These patients are usually middle aged or elderly, but increasingly children, especially those of ethnic minorities, or those who are inert and overweight, are developing Type 2 diabetes. Microvascular and macrovascular complications are frequently already present when Type 2 diabetes is diagnosed. Type 2 diabetes is commonly detected at routine medical examinations or on admission to hospital with another illness.

Adolescents

Carbohydrates, which are found in all plants, are produced from carbon dioxide and water through a process of photosynthesis [6]. There are three main forms of carbohydrates: sugars, starches, and dietary fibre, and each source is essential for the production of energy.

Adolescents, on average, consume an enormous amount of snack food that is typically quite high in sugar content. Most of their sugar supply comes from cold drinks and ice cream, sweets and pastries. Not only do these substances tend to be bad for one's teeth, but they are also implicated in obesity, behavioural disorders, diabetes mellitus, and cardiovascular disease. Thus, instead of snacking on biscuits and other such foodstuffs, we should rather be encouraging teenagers to snack on fresh fruit and nuts.

The perception of being hungry is linked to blood glucose concentration levels. When blood glucose is low, one tends to feel hungry. Snack foods that contain refined carbohydrates and sugars are quickly digested and relatively quickly absorbed leading to a rapid increase in blood sugar content and a large increase in insulin levels. This is usually followed by a rapid fall in blood glucose levels to fasting level so that the individual feels hungry, sometimes very shortly after the previous meal. This may lead to more snacking and, if this sort of eating pattern is perpetuated, obesity may result. Should a meal

contain other nutritional elements in addition to carbohydrates, however, food is more slowly digested and absorbed and it may be some hours before the individual feels ready for the next meal.

Calories

Provision of adequate calories for normal growth and development in children and adolescents with diabetes is a key component of nutrition therapy [7]. Therefore, it is important to monitor growth by measuring height and weight every 3 months and recording it on a Centers for Disease Control and Prevention (CDC) pediatric growth chart. Children do, however, appear to have the inherent ability to select appropriate amounts and type of food to sustain normal growth. Nutrition assessment tools such as 24-h recall, 3-day food records, and food frequency questionnaires can be used in conjunction with a computer nutrient analysis program to determine usual nutrient intake. Once calorie and nutrient needs are established, they can be adjusted to accommodate growth or prevent accelerated weight gain.

At the time of diagnosis, many children and adolescents with type 1 diabetes present with weight loss that must be restored with insulin initiation, hydration, and adequate energy intake. With weight loss or lack of weight gain at diagnosis, youth with diabetes usually require additional calories to promote catch-up growth. Because energy requirements change with age, physical activity, and growth rate, an evaluation of height, weight, BMI, and nutrition plan is recommended at least every year. Children and adolescents, along with their families, should be taught meal-planning basics to prevent excess weight gain. Regular physical activity should be encouraged, and children and their families should be taught the proper treatment of hypoglycemia to prevent excess caloric intake and weight gain.

Chronic undertreatment with insulin along with longstanding poor diabetes control often leads to poor growth and weight loss, whereas overtreatment with insulin can lead to excessive weight gain. In addition, impaired linear growth or poor weight gain should raise concern for the development of other related autoimmune diseases such as hypothyroidism and celiac disease and behaviors such as disordered eating behaviors or insulin omission. Evaluation of height and weight on the CDC growth curves at each clinic visit will allow for early recognition of any changes from normal, which then can be evaluated and treated.

Diabetes Insipidus

Diabetes insipidus (DI) is a condition that can result from one of several problems [8]. Central (neurogenic) DI is caused by a defect in the synthesis of antidiuretic hormone (ADH) by the hypothalamus or release from the posterior pituitary. Nephrogenic DI results from a defect in the renal tubular response to ADH, causing impaired renal conservation of water. The primary problem is excessive output of dilute urine. Neurogenic DI may be the result of primary DI (i.e., a hypothalamic or pituitary lesion or dominant familial trait), secondary DI (following injury to the hypothalamus or pituitary stalk), or vasopressinase-induced DI, which is seen in the last trimester of pregnancy (caused by a circulating enzyme that destroys vasopressin). Nephrogenic DI either occurs as a familial X-linked trait or is associated with pyelonephritis, renal amyloidosis, Sjögren's syndrome, sickle cell anemia, myeloma, potassium depletion, effects of certain drugs such as lithium or demeclocycline, or chronic hypercalcemia. A rare form of DI, termed psychogenic diabetes insipidus, is associated with compulsive water drinking. Another form of water consumption related to DI is dipsogenic diabetes insipidus, caused by an abnormality in hypothalamic control of the thirst mechanism. This condition is most often idiopathic but has been associated with chronic meningitis, granulomatous diseases, multiple sclerosis, and other widely diffuse brain diseases. Patients with this disorder have severe polydipsia and polyuria. Gestagenic diabetes insipidus is caused by an enzyme secreted by the placenta that destroys vasopressin. The condition may be treated with desmopressin (a synthetic form of ADH) if severe, but generally resolves 6-8 wk following delivery.

Except for when it follows infection or trauma, DI onset is usually insidious, with progressively increasing polydipsia and polyuria. DI following trauma or infection has three phases. In the first phase, polydipsia and polyuria immediately follow the injury and last 4-5 days. In the second phase, which lasts about 6 days, the symptoms disappear. In the third phase, the patient experiences continued polydipsia and polyuria. Depending on the degree of injury, the condition can be either temporary or permanent.

Diabetes Melitus

Diabetes mellitus (DM) affects an estimated 11 million people in the US and over 100 million worldwide [9]. Approximately 90% of these patients have type 2 or non-insulin-dependent diabetes. The remainder are classified as type 1 or insulin-dependent diabetics.

Diabetes is characterized by chronic hyperglycemia that often requires lifelong treatment. Untreated, chronic hyperglycemia eventually leads to both micro- and macrovascular complications affecting virtually every organ system. As a result, diabetics frequently present to the emergency department (ED) with complications such as severe infections, myocardial infarction (MI), stroke, renal disease, and lower extremity ischemia and skin ulcerations.

Metabolic, vascular, and neurologic disorders ensue from dysfunctional glucose transport into body cells [6]. Insulin facilitates glucose transport into cells for oxidation and energy production. Food intake, glycogen breakdown, and gluconeogenesis increase the serum glucose level, which stimulates the beta islet cells of the pancreas to release needed insulin for transport of glucose from the bloodstream into the cells. At the cellular level, insulin receptors control the rate of transport of glucose into the cells. As glucose leaves the blood, serum levels return to normal (70-100 mg/dL).

Individuals with DM have impaired glucose transport because of decreased or absent insulin secretion and/or ineffective insulin receptors. Carbohydrate, fat, and protein metabolism are abnormal, and patients are unable to store glucose in the liver and muscle as glycogen, store fatty acids and triglycerides in adipose tissue, or transport amino acids into cells normally. DM is classified into the following four clinical classes including prediabetes.

Prediabetes

Many people who eventually develop diabetes have blood glucose that is higher than normal but not high enough to establish a diagnosis of diabetes (although the cut-off is arbitrary) [10]. This condition is closely associated with visceral obesity, and in particular with deposition of adipose tissue in the abdominal region (as opposed to the hips and buttocks), and is associated with metabolic syndrome. This borderline abnormality in blood glucose and glucose tolerance testing is termed prediabetes to indicate that increased beta cell insulin production can no longer completely keep pace with the increasing resistance of insulin targets to the effect of the hormone. Reducing the demands on the pancreas can be accomplished by weight loss and moderate exercise (which reduce the insulin resistance of body cells so less insulin is required) and by healthy eating habits emphasizing fruits, vegetables, and whole grains (called the "Mediterranean-style diet"). Certain medications (such as metformin, which inhibits the production of glucose by the liver) may also be required. All these measures help preserve beta cell function and promote more efficient utilization of glucose so that blood glucose does not rise as high after eating.

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a life-threatening condition caused by severe lack of effective insulin, resulting in major hyperglycemia and metabolic, anion-gap acidosis from abnormal carbohydrate, fat, and protein metabolism resulting in production of ketones [8]. The intracellular environment is unable to receive necessary glucose for oxidation and energy production without insulin to facilitate transport of glucose from the bloodstream across the cell membrane. Impairment of glucose uptake results in hyperglycemia, while the intracellular environment continues to lack necessary nutrients. Glucagon secretion increases, causing available body stores of food substances to be broken down in an attempt to provide cell nourishment. Impaired amino acid transport, protein synthesis, and protein degradation facilitate protein catabolism with a resultant increase in serum amino acids, while fat breakdown results in elevated free fatty acids (FFAs) and glycerol. The liver converts the newly available amino acids, fatty acids, and glycerol into glucose (gluconeogenesis) in an attempt to provide nourishment for the cells, but instead the hyperglycemia worsens because of the lack of insulin to transport glucose into the cells. The liver also produces ketone bodies from available FFAs, causing mild to severe acidosis. As ketone bodies increase in the extracellular fluid, the hydrogen ions within the ketones are exchanged with K ions from within the cells. Thus, intracellular K^+ is released into the extracellular fluid and therefore to circulating fluid, where it is excreted by the kidneys into the urine. Hyperglycemia acts as an osmotic diuretic, causing severe fluid and electrolyte losses, leading to hypovolemic shock if untreated. Individuals with severe DKA may lose nearly 500 mEq of Na^+ , Cl^- , and K^+ , along with approximately 7 L of water in 24 hr.

Prediction

It is the predictable pattern of diseases, both in their natural history and in their response to therapy, which has been the cornerstone of modern medicine [11]. The early induction of diabetes-associated autoantibodies and the long pre-diabetic period suggested the possibility that autoimmune diabetes could be predicted. Indeed, autoantibodies, which appear in the peripheral blood long before clinical symptoms, are more reliable predictive markers than the presence of high-risk genes, not only in diabetes but also in a substantial number of other autoimmune diseases.

If an autoantibody is used to predict a disease, then three criteria must be fulfilled: first, every non-diseased subject with the autoantibody would eventually develop the disease (high disease-positive predictive value); second, every non-diseased subject with the autoantibody would develop the associated disease and not any other disease (high disease specificity); and third, every subject who developed the disease would have that particular autoantibody (high disease sensitivity). The positive predictive value is higher the greater is the population risk of developing the disease (disease risk). The feasibility of screening for autoantibodies as predictors of disease has been convincingly demonstrated over the last few years in the case of T1DM (Type 1 diabetes mellitus). International workshops have demonstrated the validity of assays, in terms of consistency and accuracy, for certain antigen-specific autoantibodies. Using these assays, the positive predictive value for diabetes increases for one, two, or three autoantibodies from approximately 10 to 50 and 80%, respectively, within 5 years and even higher thereafter.

As before, there is a caveat that our ability to predict autoimmune diabetes in childhood-onset disease has yet to be demonstrated in adult-onset cases. If the immune process associated with the development of T1DM is sometimes initiated later in life, then population screening will have to be performed at different ages to detect induction of diabetes-associated autoantibodies in the pre-diabetic period. Indeed, as autoantibodies to different antigens appear sequentially, and the predictive value of an autoantibody combination varies with age, disease-risk based on autoantibody combinations will require repeated screening with different combinations. Thus, screening strategies will need to be flexible.

Conclusion

Glucose is a simple sugar that is found in food as such and is released during digestion or is released from the liver. This sugar is the basic source of energy for the proper functioning of the human body. During the process of digestion in the small intestine, complex carbohydrates are decomposed and the glucose thus released is transported through the cells of the small

intestine into the bloodstream and thus it reaches all the cells of the body. Glucose cannot enter the cells on its own, it needs the help of insulin. Without insulin, cells are left without energy from sugar, although there is enough of it in the bloodstream, so in certain types of diabetes we have an ironic situation - the cells are starving in the middle of abundance. Excess sugar is "stored" in the liver in the form of glycogen and is released again during starvation. Insulin is a hormone secreted by β cells of the pancreas. This hormone helps sugar enter the cells and regulates its level in the blood. After a meal, blood glucose levels rise In response to elevated blood glucose levels, the pancreas releases insulin to allow cells to use this source of energy and to regulate blood sugar levels. When the blood sugar level drops, insulin secretion stops. Diabetes occurs when the pancreas does not produce enough insulin and/or when the body's cells do not recognize insulin, so the transfer of sugar from the blood to the cell becomes impossible. Decreased insulin production occurs due to the breakdown of pancreatic β cells either due to autoimmune processes or the action of some other factors. It is believed that the manifestation of this metabolic disorder occurs when the number of β cells are reduced to one third.

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