ScieniQ Publishers

Journal of Diabetes & Metabolic Disorders

Research Article

A Few Words about Type 1 Diabetes

Siniša Franjić

Independent Researcher, Europe

***Corresponding author**
Siniša Franjić, Independent Researcher, Europe

Submitted: 04 Apr 2021
Accepted: 06 Apr 2021
Published: 14 Apr 2021

Abstract
In addition to insulin and blood sugar control, proper nutrition and physical activity play an important role in treatment. Regular exercise is one of the most important measures in the treatment and regulation of diabetes in both type 1 and type 2. Elevated blood glucose levels or hyperglycemia can have long-term effects on the body, so we talk about late or chronic complications of diabetes that occur after longer duration of the disease. Primary damage to small blood vessels occurs primarily due to prolonged high blood sugar levels and they initially manifest on the eyes, kidneys, and nerves. Continuous education of patients with diabetes and its environment is one of the most important methods by which the patient is motivated and given constant support in insisting on the best possible control of the disease to delay or prevent late complications of diabetes.

Keywords: Diabetes, Type 1, Type 2, Insulin, Health

Introduction
Type 1 diabetes (T1D) is due to destruction of B-cells in the pancreatic islets of Langerhans with resulting loss of insulin production [1]. A combination of environmental and genetic factors that trigger an autoimmune attack on the B-cells is responsible, occurring in genetically susceptible individuals. Thus, among monozygotic identical twins only about one-third of the pairs are concordant for diabetes in contrast to the situation in Type 2 diabetes where almost all pairs are concordant. The process of islet destruction probably begins very early in life and is known to start several years before the clinical onset of diabetes.

As the prevalence of diabetes continues to grow worldwide, disease-related morbidity and mortality are emerging as major health care problems [2]. Epidemiologic evidence suggests the relationship between diabetes and complications begins early in the progression from normal glucose tolerance to impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) to diabetes than previously thought. These observations indicate that early identification and management of individuals with diabetes and prediabetes have the potential to reduce both the incidence of diabetes and its related complications.

The global incidence of T1D in children and adolescents is rising with an estimated overall annual increase of approximately 3%. The increase in incidence of T1D has been shown in countries having both high and low prevalence figures, with an indication of a steeper increase in some of the low-prevalence countries. Several European studies have suggested that, in relative terms, the increase is more pronounced in young children. Although T1D usually accounts for only a minority of the total burden of diabetes in a population, it is the predominant form of the disease in younger age groups in most developed countries.

T1D results from the autoimmune destruction of insulin-producing beta cells in the pancreas. Genetic, metabolic, and environmental factors act together to precipitate the onset of the disease. The excess mortality associated with complications of T1D and the increasing incidence of childhood T1D emphasize the importance of therapeutic strategies to prevent this chronic metabolic disorder. Increasingly, efforts need to be directed toward early diagnosis of T1D because it is a condition leading to early complications, and the potential availability of disease-modifying interventions underscore the need for early diagnosis.

Pathogenesis
Type 1 diabetes is an autoimmune disease in which cytotoxic CD8+ T lymphocytes attack and destroy the pancreatic islets [3]. The production of autoantibodies to beta cell products and components including insulin accompanies beta cell destruction. Such antibodies may be found before there is any evidence of clinical disease. The rate at which islets are destroyed by the immune system and the rate at which insulin secretion

declines varies among affected individuals, but the disease usually has a long onset with severe disease being present after about 80 percent of beta cells are destroyed. In some cases, onset may be so slow as to not be noted until adulthood (LADA). However, the peak incidence of T1DM occurs primarily in children and young adults, most often around puberty. There is a clear hereditary predisposition to type 1 diabetes. People who inherit certain HLA-D types are at increased risk of acquiring this type of diabetes as well as other autoimmune diseases of the endocrine system. (HLA types and predisposition to disease are considered in the discussion on immunology.) Other nongenetic factors are also important in the causation of T1DM. More than 80 percent of patients do not have an affected relative, and fewer than half of identical twins both develop the disease. Seasonal variation in frequency and changes in the frequency of T1DM with time in a population suggest that environmental agents (and in particular infectious disease) may have a role in T1DM etiology. Infection with Coxsackie B virus has been noted to precede some cases of the disease.

The pathogenesis of T1DM is clearly related and proportional to the lack of insulin and consequent metabolic changes associated with it. Uncontrolled hepatic glucose output and lack of storage into muscle and fat tissue leads to high blood sugar (hyperglycemia). The osmotic effect (hyperosmolarity) leads to excessive urination (polyuria) with dehydration, increased thirst (polydipsia), and loss of minerals. The person with type 1 diabetes, lacking insulin, is unable to use carbohydrates because insulin is required to promote entry of glucose into the cells where the glucose can be metabolized to yield energy. Metabolism falls into a starvation-like state. Adipose stores are used as an energy source, and the oxidation of fat produces ketone bodies, which are released from the liver into the blood, leading to metabolic acidosis (diabetic ketosis). Together the acidosis, dehydration, and loss of ions can lead to coma and ultimately death if left untreated by provision of exogenous insulin.

T1DM is characterized by the sudden onset of severe symptoms associated with the absolute deficiency of insulin secretion, tendency to ketosis and dependence on exogenous insulin to sustain life [4]. Represents around 10% of all cases of diabetes and is one of the most common chronic childhood conditions. T1DM is an autoimmune condition in which the immune system is activated to destroy the pancreatic cells which produce insulin. The cause of this auto-immune reaction is unknown. T1DM is not linked to modifiable lifestyle factors. There is no cure and it cannot be prevented yet.

The histopathology of T1DM is defined by a decreased beta cell mass in association with insulitis, a characteristic lymphocytic infiltrate limited to Langerhans islets and prominent in early stage of the disease in children. It has similar characteristics with autoimmune inflammatory processes found in certain thyroid diseases (thyroiditis) and adrenal (adrenalitis). Insulitis is characterized by infiltration and resulting disruption of islets with destruction of beta cells by T lymphocytes of various types.

Type 1 diabetes (T1D) is considered a multifactorial, chronic, autoimmune disease in which autoreactive T-lymphocytes cause severe loss of pancreatic beta cells [5]. Much progress has been done in the discovery of disease-predisposing genes, the identification of islet cell autoantigens, and key features of islet autoimmune responses. There is growing evidence for contributing environmental factors, including viruses, the microbiome, and dietary factors. Recent studies suggest that autoimmune-mediated beta cell destruction is likely the key pathogenic mechanism, but over a prolonged period of time, extending beyond clinical diagnosis. It is becoming evident that chronic beta cell inflammation is also a key component of the disease pathogenesis. Moreover, beta cell dysfunction is likely to precede and coexist with beta cell destruction, and it is emerging as a significant contributor to the onset of symptomatic diabetes. Thus, chronic islet inflammation and beta cell dysfunction should be considered critical therapeutic targets, together with improved immunoregulation. Growing evidence that beta cell destruction at diagnosis may only be partial in many patients is raising questions about the dynamics of the autoimmune process; the persistence of beta cells, insulin secretion, and disease activity for years after diagnosis point at the chronicity of T1D and suggest that therapeutic intervention to halt the disease process may be possible beyond the traditional, but arbitrary, immediate postdiagnosis period.

Unstable Diabetes

Blood glucose concentrations inevitably oscillate considerably over 24 hours in many Type 1 diabetic patients [1]. If these swings are used as a definition of instability then such patients might be classified as unstable. Indeed the ardent desire of some doctors to "stabilise" these patients sometimes leads the patient to undertake innumerable blood tests, to keep obsessional records, and to make themselves thoroughly miserable. The failure to succeed leads to recriminations, admissions to hospital, and absence from work. This form of physicianinduced, unstable diabetes is made worse by the inappropriate use of home blood glucose monitoring. It needs considerable patience to unravel the effects of such advice, but a more relaxed approach, together with fewer tests, can have a remarkably beneficial effect.

Very unstable diabetes (sometimes described as "brittle") disrupts the lives of a small group of insulin treated diabetic patients, with repeated admissions to hospital due either to hypoglycaemia or ketoacidosis. Homelife, school, and work are totally disrupted. With very few exceptions, this is probably not a special type of diabetes; it most commonly occurs in teenage girls, it is almost always temporary, and problems appear to vanish as life itself stabilises with employment or marriage.

Whereas type 1 diabetes used to be a lethal condition because of the development of ketoacidosis, patients with this disorder nowadays can be treated with insulin, and this approach has dramatically improved outcome [6]. Already in the late nineteenth century, dysregulated glucose homeostasis also appeared to be a hallmark of critical illness (CI). Indeed, hyperglycemia commonly develops during several types of CI, irrespective of previously diagnosed diabetes, and has long been considered an adaptive and beneficial stress response. However, it is becoming increasingly clear that the development of hyperglycemia is detrimental to the critically ill patient. Moreover, a recent large prospective randomized trial clearly demonstrated a plethora of clinical benefits of strict blood glucose control with intensive insulin therapy with, most strikingly, an almost 50% reduction in mortality.

Diabetic ketoacidosis (DKA) is the most common acute life-threatening complication of diabetes [7]. It is more commonly seen in type 1 diabetes but may occur in type 2. Patients with type 1 DM have an absolute insulin deficiency. When the production of insulin in the pancreas fails, the decreased glucose utilization creates a relative state of starvation. Counter-regulatory hormones (cortisol, glucagon, catecholamine, and growth hormone) that help maintain blood glucose levels adequate for cellular function during fasting are stimulated. These hormones promote gluconeogenesis and glycogenolysis, increasing glucose levels, and lipolysis, which converts adipose to free fatty acids. Without insulin to allow cellular absorption of glucose, these mechanisms continue to produce glucose. Severe dehydration and electrolyte losses develop as the kidneys filter the highly osmotic glucose. Furthermore, free fatty acids that cannot enter the citric acid cycle without insulin are oxidized into ketones. These accumulate to cause metabolic acidosis, further electrolyte derangement, and exocrine pancreatic dysfunction.

Insulin

People with type 1 diabetes make very little insulin or no insulin at all [8]. People with type 1 diabetes must take insulin shots in order to live. In contrast, people with type 2 diabetes and women with gestational diabetes do make insulin. But for some reason the cells in their bodies are resistant to the action of insulin or their bodies don't make enough insulin. In all types of diabetes, the glucose does not get into the cells that need it and builds

up in the bloodstream instead.

About half of the time, type 1 diabetes starts during childhood or the early teenage years. For this reason, it used to be called juvenile-onset diabetes. If your symptoms first appeared during your early teenage years, your health care provider probably suspected diabetes right away. If you were a young child when the disease developed, it might have occurred so fast that you went into a coma, before anyone suspected diabetes. Type 2 diabetes most often develops in adulthood and used to be called adult-onset diabetes. Usually, it does not appear suddenly. Instead, you may have no noticeable symptoms or only mild symptoms for years before diabetes is detected, perhaps during a routine exam or blood test. Gestational diabetes only appears during pregnancy in women with no previous history of type 1 or type 2 diabetes and usually goes away after pregnancy. Pregnant women are tested for gestational diabetes, usually during the 24th week of gestation. After pregnancy, 5 to 10 percent of women with gestational diabetes are diagnosed with type 2 diabetes. Women who develop gestational diabetes have a 20 to 50 percent risk of developing type 2 diabetes in the next 5 to 10 years.

Alcohol

Inhibition of gluconeogenesis, reduced hypoglycemia awareness due to cerebral effects of alcohol, and/or impaired counterregulatory responses to hypoglycemia have been reported as possible causes [9]. Five of six men with type 1 diabetes had dinner at 6:00 p.m. followed by drinking wine (70 g alcohol, 20 oz) or water at 9:00 p.m. After drinking wine, treatment for hypoglycemia was required after breakfast; growth hormone was significantly reduced, with no other differences in insulin or other hormone levels. Similarly, in adults with type 1 diabetes, hypoglycemia (blood glucose 50 mg/dL) resulted in lower peak growth hormone levels compared to placebo; however, this result was also associated with a decrease in insulin sensitivity. After drinking alcohol, based on continuous glucose monitoring data, individuals reported more than twice as many hypoglycemic episodes throughout the next 24 h than after drinking orange juice.

In people with type 1 diabetes, both mild alcohol intoxication and hypoglycemia (blood glucose ~43 mg/dL) were associated with deterioration in reaction time and other tests of cognitive function, and the total impairment was greater when both were experienced together. Individuals also must be aware that the effects of alcohol and hypoglycemia on cognitive function are additive and significant even after small quantities of alcohol. It is important to completely avoid alcohol when driving.

Elevated total ketone body concentrations are characteristic of both diabetic ketoacidosis (DKA) and alcoholic ketoacidosis (AKA). However, DKA compared to AKA is characterized by a higher glucose concentration and a lower b-hydroxybutyrate–to–acetoacetate and lactate-to-pyruvate ratios. Hormonal profiles are similar with decreased insulin levels and elevated levels of counterregulatory hormones. Liberal lunchtime ingestion of alcohol by patients with type 1 diabetes compared to placebo resulted in postprandial b-hydroxybutrate levels being elevated with alcohol and suppressed with placebo. The authors suggest that "binge" drinking may increase the risk of significant ketosis, especially if insulin administration is erratic. They recommend that patient education materials contain information to highlight these potential problems.

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 [10]. 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

In type 1 diabetes, the pancreas does not produce insulin at all because its beta cells, which make it, are destroyed. This is caused by autoimmune reactions in which the immune system considers beta cells to be a foreign body and attacks or destroys them. A viral infection can lead to an autoimmune reaction. In this condition, the blood glucose level rises uncontrollably and the body is deprived of the main source of energy. This leads to fatigue, lack of energy, frequent urination, dehydration, thirst and weight loss. Type 1 diabetes occurs in childhood or early adulthood and rarely develops after the age of 40. Type 1 diabetes is impossible to prevent. It does not occur all at once, but the destruction of beta cells is a process that can take months and years, and diabetes occurs only after beta cells work at less than ten percent of capacity.

References

1. Watkins, P. J. (2003.) ABC of Diabetes, Fifth Edition", BMJ Publishing Group Ltd, London, UK, pp. 2.; 30.
2. Guglielmi, C.; Pozzilli, P. (2011.) Early diagnosis of type 1 diabetes: Useful or a phyrrhic victory?" in Vella, A.; Rizza, R. A. (eds): „Clinical Dilemmas in Diabetes", John Wiley & Sons Ltd, Chichester, UK, pp. 11.
3. Reisner, E. G.; Reisner, H. M. (2017.) Crowley's An Introduction To Human Disease - Pathology and Pathophysiology Correlations, Tenth Edition", Jones & Bartlett Learning, Burlington, USA, pp. 593.
4. Puchulu, F. M. (2018.) Definition, Diagnosis and Classification of Diabetes Mellitus" in Sabban, E. N. C.; Puchulu, F. M.; Cusi, K. (eds) Dermatology and Diabetes", Springer International Publishing AG, Cham, Switzerland, pp. 9.
5. Pugliese, A. (2018.) Pathogenesis of Type 1 Diabetes" in Diabetes" in Bonora, E.; DeFronzo, R. A. (eds) Diabetes - Epidemiology, Genetics, Pathogenesis, Diagnosis, Prevention, and Treatment", Springer International Publishing AG, Cham, Switzerland, pp. 141: 142.
6. American Diabetes Association (2005) Complete Guide to Diabetes, Fourth Edition, Completely Revised", American Diabetes Association, Inc., Alexandria, USA, pp. 4.
7. Huecker, M. R.; Danzl, D. F. (2011) Metabolic & Endocrine Emergencies" in Stone, C. K.; Humphries, R. L. (eds) CURRENT Diagnosis And Treatment Emergency Medicine, Seventh Edition", The

McGraw-Hill Companies, New York, USA, pp. 780.
8. Vanhorebeek, I.; Van den Berghe, G. (2008) Intensive Insulin Therapy for the Critically Ill Patient“ in LeRoith, D.; Vinik, A. I. (eds) Controversies in Treating Diabetes - Clinical and Research Aspects“, Humana Press, Totowa, USA, pp. 158.
9. Franz, M. J.; Evert, A. B. (eds) (2012) American Diabetes Association Guide to Nutrition Therapy for Diabetes, Second Edition“, American Diabetes Association, Inc., Alexandria, USA, pp. 79: 80.
10. Beyan, H.; Leslie, D. G. (2008) Type 1 Diabetes Mellitus“ in Weetman, A. P. (ed): „Autoimmune Diseases in Endocrinology“, Humana Press, Totowa, USA, pp. 290: 291.

Cite this article: Siniša Franjić (2021) A Few Words about Type 1 Diabetes. Journal of Diabetes & Metabolic Disorders 1: 10-13.