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REVIEW ARTICLE

DIABETES MELLITUS: TYPES, DIAGNOSIS, TREATMENT CAN TYPE II DIABETES BE CURED?

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ABSTRACT

Pathogenesis of diabetes is complex and there is an interplay between genetic and environmental factors. While it is impossible to change genetic conditions at present, we do have an impact on the environmental ones. Symptoms of both Type 1 & Type 2 diabetes usually increase slowly, and therefore the patient does not pay attention to them for a long time. If diabetes is diagnosed early, and treatment is carefully planned and carried out, it is possible in many cases to achieve recovery from the clinical symptoms. Nowadays we have many modern drugs available that greatly facilitate good metabolic alignment of Type 1 & Type 2 diabetes, but till 90s pharmacological treatment was limited to insulin, metformin and sulfonylurea. Treatment for Type 1 & Type 2 diabetes must be undertaken with a view to reducing insulin resistance. Studies show that proper diet and physical activity are much more effective in preventing the development of Type 1 & Type 2 diabetes than any drug available and they are both first treatment of choice. If this is not satisfactory, or if the patient is unsuccessful, pharmacotherapy is needed. Metformin is most often used at the beginning. If the treatment applied does not give satisfactory results, it is necessary to extend the pharmacotherapy – in this case, incretin drugs and Sodium-glucose linked transporter type 2 inhibitors (SGLT2 inhibitors) are recommended. Acarbose preparations (alpha- glucosidase inhibitors) are also used as supportive treatment. Currently, drugs from the sulfonylurea group are being introduced less and less often, as their use may cause hypoglycemic conditions as well as weight gain. When the use of oral medications appears to be insufficient for metabolic control, the inclusion of injections of insulin is considered.

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INTRODUCTION

There is an interplay between genetic and environmental factors in the pathogenesis of Diabetes Type 1 & Type 2 . While it is impossible to change genetic conditions at present, we do have an impact on the environmental ones. Insulin resistance is a very important factor leading to the clinical manifestation of diabetes (1,2), for which abdominal obesity is a very important determinant. We call this condition a metabolic syndrome (3,4,5,6). Waist circumference (WC) measurement, waist/hip ratio (WHR) and waist/body height (WHtR – waist/height ratio) are used to assess abdominal obesity. According to the International Diabetes Federation 2005 criteria (IDF/2005 criteria), abdominal obesity in adults is diagnosed by adopting a waist circumference of 80 cm and 94 cm for women and men, respectively (7).

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Excessive increase in fat cells during childhood can contribute to the development of obesity in adulthood. The increasing number of fat cells is unfortunately an irreversible process (8). They accumulate not only in the subcutaneous and visceral tissues, but also in various organs, mainly in the liver, skeletal muscle, pancreas, blood vessels, heart, and kidneys. They change the cells' metabolism, and thus disrupt their proper functioning (9). The adipose tissue is a very important secretory organ. In the development of insulin resistance, bioactive substances secreted are of substantial significance. They have endocrine, paracrine, and autocrine effects, causing tissue resistance to endogenous insulin. One of these substances is adiponectin, which has many functions in our body (10). It plays an important role in maintaining insulin sensitivity of tissues, especially muscles, as well as of the liver and the adipose tissue itself. It activates fatty acid oxidation and increases insulin secretion. At the same time, apart from adiponectin, other substances are secreted by the adipose tissue, such as leptin, tumor necrosis factor α (TNF-α), interleukin 6

(IL-6), resistin, and, above all, the product of lipolysis – free fatty acids (FFA), all of which are key to the development of insulin resistance (11) of Type 1 & Type 2 diabetes. There are three main types of diabetes:

- Type I (1) diabetes
- Type II (2) diabetes
- Gestational diabetes

Type 1 Diabetes : This type of diabetes is often called juvenile-onset diabetes mellitus because it tends to start at a younger age, usually around the age of 14 years, although it may develop earlier or later in life. Type 1 diabetes is a result of destruction of the beta cells in the pancreas thereby impairing insulin production. Types 1 diabetes is an autoimmune disease which means that they body's immune cells attack and destroy the beta cells. There are various theories about the causes of this immune dysfunction but the exact cause in every case is unknown. It is believed that there is a hereditary tendency (genetic/inherited) for the beta cells to degenerate and prevent the immune cells from attacking it. This may also be linked to viruses or environmental factors. Type 1 diabetes tends to develop very abruptly, over days or weeks. The destruction of the beta cells is extensive and little or no insulin is produced therefore insulin needs to be administered (injection). Type 1 diabetes is an autoimmune condition that occurs when the body's immune system attacks the beta cells living in the tissue of the pancreas. This causes the pancreas to produce little to no insulin, which is a hormone that allows cells to use glucose for energy. Insulin makes sure the body's blood sugar levels do not get too high or too low. People with type 1 diabetes do not have a properly functioning pancreas and cannot properly distribute glucose to cells in the body. The causes of autoimmunity are unknown. Experts have linked several triggers to autoimmunity, such as stress, a diet high in refined sugars and carbohydrates, a lack of physical exercise, poor sleeping habits, and excessive smoking or drinking. Certain genetic factors may also increase the risk of autoimmunity. Autoimmune conditions tend to run in the family. A person with a family history of any autoimmune disorder, not just type 1 diabetes, may be at an increased risk. Certain viruses or illnesses may also be linked to type 1 diabetes.

Type 2 Diabetes : This type of diabetes is also known as adult-onset diabetes because it tends to occur later in life, usually after the age of 30. These days however, type 2 diabetes is being seen in younger age groups, even in adolescents. With type 2 diabetes, the impairment of glucose metabolism arises as a result of a decreased sensitivity to insulin by the body's cells. This means that the cells do not respond to insulin to take up glucose from the bloodstream and utilize it. This is known as insulin resistance. Unlike in type 1 diabetes, the insulin levels in the blood are elevated, above the norm **(**hyperinsulinemia**)** as the pancreas secretes higher amounts of glucose in an attempt to overcome this resistance (compensatory mechanism). Type 2 diabetes has been linked to a number of factors, of which obesity (especially the accumulation of abdominal fat) is now considered as the main risk factor. The rising incidence of obesity globally, especially in children and young adults, may account for type 2 diabetes being seen in younger age groups than was previously the case. Other factors that contribute to the development of type 2 diabetes includes a family history of diabetes, previous history of gestational diabetes (pregnant women), sedentary lifestyle and ethnicity. Type 2 diabetes develops gradually as the cells resistance to insulin increases over time. Despite the resistance, the cells do take up glucose but in much smaller quantities and only in the presence of very high levels of insulin. Eventually the beta cells become "exhausted" and insulin production and secretion drops. Type 2 diabetes is ultimately caused by insulin resistance, which is due to a combination of lifestyle and genetic factors. Being overweight, having an improper diet that includes excessive amounts of foods high in refined sugar and carbohydrates, and a lack of physical activity may also cause type 2 diabetes. Because type 2 diabetes is not an autoimmune disease, it does not occur as a result of an immune system dysfunction like Type 1 diabetes does. Type 2 diabetes accounts for up to ninety-five percent of diabetes cases. It tends to run in the family and is more prevalent in the following ethnic groups: Latinos, African Americans, Native Americans, Pacific Islanders, and Asian Americans. Women who have been diagnosed with gestational diabetes have a higher risk of developing type 2 diabetes within ten years. It is estimated that one in three adults in the United States will have type 2 diabetes by the year 2050.

Gestational Diabetes: This type of diabetes develops in some women in late pregnancy and usually resolves after the birth of the baby. It can however persist and become permanent. Even if gestational diabetes resolves, the mother is at an increased risk of type 2 diabetes as mentioned above. The baby is also at a higher risk of type 2 diabetes if born to a mother who had gestational diabetes. The main causes of gestational diabetes appear to be related to the hormone fluctuations associated with pregnancy as well as excessive weight gain during pregnancy. Obese women who fall pregnant are at a greater risk as well as certain ethnic groups and women who were diagnosed with pre-diabetes (impaired glucose tolerance) prior to pregnancy. Apart from increasing the baby's risk of developing type 2 diabetes later in life, gestational diabetes may also increase body fat in the baby (large baby requiring cesarean section), cause low blood sugar levels (hypoglycemia) in the baby or breathing problems **(**neonatal breathing problems**).** Recently, a report on leptin-induced epigenetic modifications as well as epigenetic regulation of leptin in metabolic disorders has been published (12). One of the important elements in the development of insulin resistance is the increased synthesis and release of proinflammatory cytokines, which also cause damage to pancreatic islet cells (13,14). Decreased insulin sensitivity can be seen many years before Type 2 diabetes is diagnosed. Insulin resistance can lead to a number of disorders including the metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and Type 2 diabetes (15,16,17). Micro and macro-vascular complications are very aggravating complications of insulin resistance. Experimental studies have shown that fat storage in the heart can lead to cardiomyocyte necrosis, and affect myocardial contractility. A relationship between insulin resistance and myocardial damage has been observed in clinical studies (18,19,20,21,22). An increased influx of free fatty acids can also cause kidney damage (23), whereas the accumulation of fat in the liver cells can lead to chronic inflammation and fatty liver. The relationship between metabolic syndrome and periodontal changes has also been discussed in the literature – Gurav has introduced and elaborated on these issues extensively (24,25,26,27,28,29,30,31,32). The author has noted the importance of early diagnosis of this complication.

The LJM (limited joint mobility) syndrome may also be an early complication signaling the diagnosis of diabetes (33,34). Diabetic patients often have accompanying endocrine disorders, including thyroid dysfunction (35). Endocrinologist care is needed in such cases.

SYMPTOMS

Common symptoms of type 1 diabetes include weight loss, extreme thirst, frequent urination, and dehydration. Other symptoms may include bedwetting, blurry vision, a rapid heartbeat, fatigue, vomiting, and nausea. Symptoms usually come on fairly quickly within a few days to a few weeks. Extreme hunger, mood changes, irritability, and food cravings may also occur. Lightheadedness when standing up may also occur due to low blood sugar levels. Numbness or tingling in the legs is an early symptom of diabetes. Type 1 diabetes is diagnosed by checking for high blood sugar levels and the presence of ketones, which are the byproducts of the breakdown of fat. A doctor may order a HbA1c test to determine blood sugar levels over the past three months. A random blood sugar test or a fasting blood sugar test may also be done. A doctor may diagnose type 1 diabetes by performing an antibody test or checking C-peptide levels, which is the byproduct of insulin in the pancreas.

The most common symptoms of type 2 diabetes include weight gain or weight loss, blurry vision, poor wound healing, excessive thirst, fatigue, and excessive hunger. Obesity increases the risk of type 2 diabetes; however, during the early stages of type 2 diabetes, a person may experience unexplained weight loss. Food cravings tend to occur because the body's cells are not getting the glucose they need, which increases the need for glucose consumption. A physician can diagnose type 2 diabetes using a random blood test, an oral glucose intolerance test, a fasting blood sugar test, or a HbA1c test. A blood test may need to be conducted more than once before a diagnosis can be made. In some cases, several different blood tests may be ordered before making a diagnosis. A blood test may be ordered if a patient has a family history of diabetes and experiences one or more symptoms. Symptoms of Type 2 diabetes usually increase slowly, and therefore the patient does not pay attention to them for a long time. Unfortunately, the disease is usually diagnosed when chronic complications occur. This is already a period in which it is often impossible to reverse the symptoms of the disease. It is very important to systematically carry out glucose tolerance tests (OGTT) for people at high risk of the disease. The risk group includes people with obesity, hypertension, and heart disease, as well as with a family history of diabetes. It is worth mentioning that for early diagnosis of glucose tolerance disorders it is very useful to determine blood sugar levels in the glucose tolerance test also one hour after loading (36,37,38). The main difference between type 1 and type 2 diabetes is that type 2 diabetes is not an autoimmune condition. In many cases, type 2 diabetes can be reversed. It is a chronic disease that affects that body's ability to use glucose. Type 2 diabetes results from insulin resistance or a condition that is characterized by difficulty using insulin correctly. People with type 2 diabetes may also experience abnormal insulin secretion, which causes glucose to build up in the bloodstream. Both forms of diabetes are equally dangerous.

DAIGNOSIS: Despite very distinct symptoms, both types of diabetes can be mistaken for lingering flu symptoms or other ordinary illness that doesn't require treatment.

It's crucial that anyone displaying signs of diabetes have their blood sugar levels tested and urine tested for ketones. According to the American Diabetes Association, the following blood sugar and A1c results are used to diagnose prediabetes and type 2 diabetes.

Prediabetes

- HbA1c: 5.7 to 6.4 percent
- Fasting: 100 to 125 mg/dL
- 2 hours after a meal: 140 mg/dL to 199 mg/dL

Too often, patients diagnosed with prediabetes are simply sent home and given very little guidance on what they can do to prevent the further development of type 2 diabetes. Consider your prediabetes diagnosis as a tremendous warning that type 2 diabetes is imminent unless you take action by making changes in your nutrition, body weight, and activity levels to help compensate for your body's struggle to produce adequate insulin. For some, losing weight and eating differently *cannot* prevent the development of type 2 diabetes, but for many, it can.

Type 2 diabetes

- HbA1c: 6.5 percent or higher
- Fasting: 126 mg/dL or higher
- 2 hours after a meal: 200 mg/dL or higher

Some patients diagnosed with type 2 diabetes can actually have type 1 diabetes. This mistake can happen in adults developing type 1 because many doctors aren't aware of how common type 1 diabetes has become in adults. If you've been diagnosed with type 2 and you suspect you actually have type 1, ask to have your autoantibody levels tested. This test will reveal if your body is struggling with an autoimmune form of diabetes versus a metabolic disorder.

Type 1 diabetes

- HbA1c: 6.5 percent or higher
- Fasting: 126 mg/dL or higher
- 2 hours after a meal: 200 mg/dL or higher

For patients with undiagnosed type 1 diabetes, blood sugar levels are often above 400 mg/dL before they've made a visit to the emergency room or primary care. If you do suspect that you or someone you know has type 1 diabetes, visit your primary care or urgent care immediately. Be sure to ask for both your blood sugar level and your urine ketone level to best tested.

Type 1 or type 2 diabetes are all encouraged to achieve an HbA1c level at or below 7.0 percent for the best prevention of diabetes-related complications.

TREATMENT

The basic principle of treating Type 2 diabetes is to change one's lifestyle, which means introducing a very well-defined, low-calorie diet, and maximally increasing one's physical activity, taking into account possible medical contraindications. Studies show that proper diet and physical activity are much more effective in preventing the development of Type 2

diabetes than any drug available. The diet should gradually reduce the number of calories consumed after about 500 kcal. A typical reduction diet, i.e. one that leads to a decrease in body weight, is 1000-1200 kcal/day. It is assumed that weight reduction should be at the level of 0.5-1 kg per week. If the patient does not lose weight, it means that the diet contains too many calories for the needs of their body. Of course, any diet that aims to reduce body weight should be supported by regular physical activity. If this is not satisfactory, or if the patient is unsuccessful, pharmacotherapy is needed. Metformin is most often used at the beginning. It is a drug that reduces insulin resistance. If the treatment applied does not give satisfactory results, it is necessary to extend the pharmacotherapy – in this case, incretin drugs and SGLT2 inhibitors are recommended (39,40,41,42,43,44,45).

The use of these drugs has been found to be beneficial in preventing diabetes complications (46,47,48). Wilding et al. have proposed combining the SGLT2 inhibitor with an incretin drug as a beneficial solution in preventing cardiac complications (49). Scheen has also presented the beneficial effects of combining a dipeptidyl peptidase-4 inhibitor (DPP-4 inhibitor) with an SGLT2 inhibitor in the treatment of Type 2 diabetes (50). American authors also presented a similar position (51). Acarbose preparations (alpha-glucosidase inhibitors), which facilitate weight reduction, are also used as supportive treatment (52,53,54). Currently, drugs from the sulfonylurea group are being introduced less and less often, as their use may cause hypoglycemic conditions as well as weight gain. When the use of oral medications appears to be insufficient for metabolic control, the inclusion of injections is considered. In this group of drugs, the decision to include insulin is usually the first priority. Of course, insulin is still a drug used in patients with Type 2 diabetes, but the indications for its use have changed. It should be remembered that in Type 2 diabetes, the secretion of endogenous insulin can be preserved for quite a long time, and it is often significantly increased in response to insulin resistance. The decision to start insulin therapy should be preceded by an assessment of insulin secretion. The simplest test is to determine the level of C-peptide (55,56). Currently, more and more analog insulin preparations appear on the market, which may be useful in the treatment of Type 2 diabetes (57,58), however in obese patients insulin treatment should be seen as a last resort (59). If we are dealing with very high hyperglycemia (≥ 300 mg/dl, i.e. ≥ 16 mmol/l) at the time diabetes is diagnosed with concomitant clinical symptoms. It is necessary to include insulin as soon as the diagnosis is made. Insulin therapy is often used transiently in these patients. This applies especially to the early periods of the disease when the function of β-cells is still preserved. Increasingly, when oral medications are ineffective, glucagon-like peptide-1 receptor agonist (GLP-1 RA) injections are used before insulin therapy (60). Careful monitoring of early signs of chronic complications is also very important in patients. As part of such control, the level of glycated hemoglobin (HbA1c) and lipidogram should be tested periodically. Ophthalmologic monitoring is necessary as part of specialist consultations. It is assumed that every patient with diabetes requires ophthalmologic monitoring at least once a year. All patients over the age of 35 should also consult a cardiologist before commencing intensive physical exertion.

Conclusion

The question posed in the title can be answered with "Yes" – diabetes can be cured as a clinically overt disease, provided that it is diagnosed at an early stage, that it is treated very vigorously, and, above all, that there is a definite reduction in body weight or obesity. However, one should keep in mind that genetic predispositions remain (61). If the patient is diagnosed with Type 2 diabetes late when the complications are already developed and present, the patient requires very careful diagnosis and specialized treatment with dietary changes and drugs. In that case, we can no longer expect that the clinical symptoms will disappear; at most the treatment will slow down their development. That is why it is so important to diagnose metabolic syndrome and related diseases as early as possible.

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REFERENCES

1. Czech A, Tatoń J, Piatkiewicz P. Cellular glucose transport disturbances in the pathogenesis and therapy of type 2 diabetes mellitus. Endokrynol Pol. 2010;61(3):292-302.
2. Tatoń J, Czech A, Piatkiewicz P. Insulin as the main regulator of cellular glucose utilization-aetiological aspects of insulin resistance. Endokrynol Pol. 2010;61(4):388-394.
3. Chwalba A, Otto-Buczkowska E. Metabolic syndrome is the problem in young diabetics? Fam Med Sci 2014; 3(4):2-7 ICID: 1136490 ISSN: 2327-4972.
4. Otto-Buczkowska E. Pathogenetic influence of obesity associated with insulin – resistance on the induction of the several clinical complications in children and adolescents. Med Metabol 2012;16(4):59-65. ISSN 1428-1430 ICID: 1037035.
5. Otto-Buczkowska E. Metabolic syndrome – increasing problem. Post Nauk Med. 2014;27(12B):11-16. ISSN: 0860-6196.
6. Otto-Buczkowska E, Dryżałowski M. Metabolic syndrome in young patients. PediatrEndocrinol Diabetes Metab. 2015;23(1)32-36 ISSN 2081-237X.
7. Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: A global public health problem and new definition. J.Thromb. 2005:12(6):295-300.
8. Mansyur MA, Bakri S, Patellongi IJ, Rahman IA. The association between metabolic syndrome components, low-grade systemic inflammation. Atheroscler and insulin resistance in non-diabetic Indonesian adolescent male. Clin Nutr ESPN.2020:35:69-74.
9. Knight JA. Diseases and disorders associated with excess body weight. Ann Clin Lab Sci. 2011;41(2):107- 121.
10. Ramakrishnan N, Jialal I. Biochemistry, Adiponectin. StatPearls Publishing; 2020-2018 Dec 23.
11. Otto-Buczkowska E, Chobot A. Role of ghrelin and leptin in the regulation of carbohydrate metabolism. Part II. Leptin. PostepyHig Med Dosw 2012; 66:799-803 ISSN 1732-2693 ICID: 1015534
12. Wróblewski A, Strycharz J, Świderska E, Drewniak K, Drzewoski J, Szemraj J, Kasznicki J, Śliwińska A. Molecular Insight into the Interaction between Epigenetics and Leptin in Metabolic Disorders. Nutrients. 2019; 11 (8). pii: E1872. doi: 10.3390/nu11081872.
13. Cieślak M, Cieślak M. Role of purinergic signalling and proinflammatory cytokines in diabetes. Clinical Diabetology. 2017;6(3):90-100. ISSN: 2451-0971.
14. Mahlangu T, Dludla PV, Nyambuya TM, Mxinwa V, Mazibuko-Mbeje SE, Cirilli I et al.. A systematic review on

the functional role of Th1/Th2 cytokines in type 2 diabetes and related metabolic complications. Cytokine. 2020;126:154892. doi: 10.1016/j.cyto.2019.154892.
15. Dite P, Blaho M, Bojkova M, Jabandziev P, Kunovsky L. Nonalcoholic Fatty Pancreas Disease: Clinical Consequences. Dig Dis. 2020;38(2):143-149. doi: 10.1159/000505366.
16. Freeman AM, Pennings N. Insulin Resistance. StatPearls Publishing; 2020-2019 Dec 26.
17. Szalat A, Durst R, Leitersdorf E. Managing dyslipidaemia in type 2 diabetes mellitus. Best Pract Res Clin Endocrinol Metab. 2016;30:431-444. doi:10.1016/j.beem.2016.05.004.
18. Kadakia MB, Fox CS, Scirica BM. Murphy SA, Bonaca MP, Morrow DA. Central obesity and cardiovascular outcomes in patients with acute coronary syndrome: observations from the MERLIN-TIMI 36 trial. Heart. 2011;97(21):1782-1787. doi: 10.1136/heartjnl-2011-300231.
19. Laakso M, Kuusisto J. Insulin resistance and hyperglycaemia in cardiovascular disease development. Nat Rev Endocrinol. 2014;10(5):293-302. doi: 10.1038/nrendo.2014.29.
20. Landa-Galvan HV, Rios-Castro E, Romero-Garcia T, Rueda A, Olivares-Reyes JA. Metabolic syndrome diminishes insulin-induced Akt activation and causes a redistribution of Akt-interacting proteins in cardiomyocytes. PLoS One. 2020;15(1):e0228115. doi: 10.1371/journal.pone.0228115.
21. Sun D, Man W, Zhang L. Roles of Insulin resistance, endothelial dysfunction and lifestyle changes in the development of cardiovascular disease in diabetic patients. Curr Drug Targets. 2017;18(15):1792-1799 doi: 10.2174/1389450117666160715145518.
22. Zhang PY, Xu X, Li XC. Cardiovascular disease in diabetes. Eur Rev Med Pharmacol Sci. 2014;18:2205- 2214.
23. Otto-Buczkowska E, Tucholski K. Kidneys function in glucose homeostasis regulation and its therapeutic implications. Fam Med Primary Care Rev. 2013;15:34-37. ISSN 1734-3402 ICID: 1047532.
24. Albert DA, Ward A, Allweiss P, Graves DT, Knowler WC, Kunzel C. et al. Diabetes and oral disease: implications for health professionals. Ann N Y Acad Sci. 2012;1255:1-15. doi: 10.1111/j.1749-6632.2011.06460.x.
25. Chwalba A, Otto-Buczkowska E. Oral lesions in diabetic patients – role of dental professionals in diagnostics and therapy. J Stoma. 2015; 68(2):206-217. ICID: 1156243.
26. Dye BA, Genco RJ. Tooth loss, pocket depth, and HbA1c information collected in a dental care setting may improve the identification of undiagnosed diabetes. J Evid Based Dent Pract. 2012;12(3 Suppl):12-14. doi: 10.1016/S1532-3382(12)70003-9.
27. Gurav AN. The association of periodontitis and metabolic syndrome. Dent Res J (Isfahan). 2014;11(1):1-10.
28. Lalla E, Cheng B, Kunzel C, Burkett S, Lamster IB. Dental findings and identification of undiagnosed hyperglycemia. J Dent Res. 2013;92(10):888-892.
29. López NJ, Quintero A, Casanova PA, Ibieta CI, Baelum V, López R. Effects of eriodontal therapy on systemic markers of inflammation in patients with metabolic syndrome: a controlled clinical trial. J Periodontol. 2012;83(3):267-278. doi: 10.1902/jop.2011.110227.
30. Pranckeviciene A, Siudikiene J, Ostrauskas R, Machiulskiene V. Severity of periodontal disease in adult patients with diabetes mellitus in relation to the type of diabetes. Biomed Pap Med FacUnivPalacky Olomouc Czech Repub. 2014;158(1):117-123. doi: 10.5507/bp.2013.098.
31. Zhu M, Nikolajczyk BS. Immune cells link obesity-associated type 2 diabetes and periodontitis. J Dent Res. 2014;93:346-352 doi: 10.1177/0022034513518943.
32. Gurav AN. Management of diabolical diabetes mellitus and periodontitis nexus: Are we doing enough?. World J Diabetes. 2016;7(4):50-66. doi: 10.4239/wjd.v7.i4.50.
33. Otto-Buczkowska E, Jarosz-Chobot P. Limited joint mobility syndrome in patients with diabetes. Int J Clin Pract. 2012;66(4):332-333.
34. Chwalba A, Otto-Buczkowska E. The effect of diabetes on the connective tissue and the bone-joint system. Eur J Clin Exp Med 2018; 16 (3): 233–238.
35. Chwalba A, Otto-Buczkowska E. Thyroid – The Gland That Can Not be Neglected in Diabetes Patients. Sumerianz Journal of Medical and Healthcare 2019;1(2):63-69.
36. Buysschaert M, Bergman M, Yanogo D, Jagannathan R, Buysschaert B, Preumont V. An elevated 1-h post- load glucose level during the oral glucose tolerance test detects prediabetes. Diabetes Metab Syndr. 2017;11(2):137-139. doi: 10.1016/j.dsx.2016.12.002.
37. Grzyb K, Jainta N, Otto-Buczkowska E. Increased plasma glucose level after 1 hour of challenge in the oral glucose tolerance test (OGTT) as an indicator of pre-diabetes. J Endocrinol Diab. 2018;5(3): 1-3..
38. Otto-Buczkowska E, Dryżałowski M. The utility of serum glucose measurement at 1 hour of the oral glucose tolerance test. Clinical Diabetology 2016;5(4):127-130.
39. Chao EC. SGLT-2 inhibitors: a new mechanisms for glycemic control. Clin. Diabetes,2014; 32(1):4-11. doi: 10.2337/diaclin.32.1.4.
40. Merlotti C, Moabito A, Pontiroli E. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes, Obesity and Metabolism 2014; 16(8):719-727. doi: 10.1111/dom.12270.
41. Muscogiuri G, Gastaldelli A. Albiglutide for the treatment of type 2 diabetes. DrugsToday (Barc). 2014;50(10):665-678. doi: 10.1358/dot.2014.50.10.2214156.
42. Muscogiuri G, DeFronzo RA, Gastaldelli A, Holst JJ. Glucagon-like Peptide-1 and the Central/Peripheral Nervous System: Crosstalk in Diabetes. Trends Endocrinol Metab.2017;28(2):88-103. doi: 10.1016/j.tem.2016.10.001.
43. Nauck M. Incretin therapies: highlighting common features and differences in the modes of action of glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors. Diabetes Obes Metab. 2016;18(3):203-216. doi: 10.1111/dom.12591.
44. Polish Diabetes Association recommendations for the clinical management of patients with diabetes in 2019. ClinDiabetol. 2019;8 (1) ISSN 2451–0971.
45. Shomali M.: Optimizing the care of patients with type 2 diabetes using incretin-based therapy: focus on GLP- 1 receptor agonists. Clin. Diabetes, 2014; 32(1):32-43. doi: 10.2337/diaclin.32.1.32.
46. Zelniker TA, Braunwald E. Treatment of Heart Failure with Sodium-Glucose Cotransporter 2 Inhibitors and Other Anti-diabetic Drugs. Card Fail Rev. 2019;5(1):27-30. doi: 10.15420/cfr.2018.44.1.
47. Scheen AJ. Effect of sodium-glucose cotransporter type 2 inhibitors on liver fat in patients with type 2 diabetes: hepatic beyond cardiovascular and renal protection?. Ann Transl Med. 2018;6(Suppl 1): S68. doi: 10.21037/atm.2018.10.39.
48. Scheen AJ. Cardiovascular and renal protection with sodium-glucose cotransporter type 2 inhibitors: new paradigm in type 2 diabetes management and potentially

beyond. Ann Transl Med. 2019;7(Suppl 3): S132. doi: 10.21037/atm.2019.05.82.
49. Wilding JP, Rajeev SP, DeFronzo RA. Positioning SGLT2 Inhibitors/Incretin-Based Therapies in the Treatment Algorithm. Diabetes Care. 2016; 39Suppl 2:S154-164. doi: 10.2337/dcS15-3005.
50. Scheen AJ. DPP-4 inhibitor plus SGLT-2 inhibitor as combination therapy for type 2 diabetes: from rationale to clinical aspects. Expert Opin Drug Metab Toxicol. 2016:12(12):1407-1417.
51. Triplitt C, Solis-Herrera C, Cersosimo E, Abdul-Ghani M, Defronzo RA. Empagliflozin and linagliptin combination therapy for treatment of patients with type 2 diabetes mellitus. Expert Opin Pharmacother. 2015;16(18):2819-33. doi: 10.1517/14656566.2015.1114098.
52. Holman RR, Bethel MA, Chan JC, Chiasson JL, Doran Z, Ge J. et al. ACE Study Group Rationale for and design of the Acarbose Cardiovascular Evaluation (ACE) trial. Am. Heart J. 2014;168(1):23-9.e2. doi: 10.1016/j.ahj.2014.03.021.
53. Joshi SR, Ramachandran A, Chadha M, Chatterjee S, Rathod R, Kalra S. Acarbose plus metformin fixed- dose combination in the management of type 2 diabetes. Expert Opin Pharmacother. 2014;15(11):1611-1620. doi: 10.1517/14656566.2014.932771.
54. Su B., Liu H., Li J, Sunli Y, Liu B, Liu D, Zhang P, Meng X. Acarbose treatment affects the serum levels of inflammatory cytokines and the gut content of bifidobacteria in Chinese patients with type 2 diabetes mellitus. J. Diabetes. 2015;7(5):729-739. doi: 10.1111/1753-0407.12232.
55. Otto-Buczkowska E. The clinical utility of C-peptide measurement in diabetology. Pediatr Endocrinol Diabetes Metab. 2014;20:63-68doi: 10.18544/PEDM-20.02.0004.
56. Si Y, Shen Y, Lu J, Ma X, Zhang L, Mo Y. et al Impact of acute-phase insulin secretion on glycemic variability in insulin-treated patients with type 2 diabetes. Endocrine. 2020 Jan 31.doi: 10.1007/s12020-020- 02201-y.
57. Aye MM, Atkin SL. Patient safety and minimizing risk with insulin administration - role of insulin degludec. Drug Healthc Patient Saf. 2014;6:55-67 doi: 10.2147/DHPS.S59566.
58. Haluzik M, Kretowski A, Strojek K, Czupryniak L, Janez A, Kempler P. et al. Perspectives of Patients with Insulin-Treated Type 1 and Type 2 Diabetes on Hypoglycemia: Results of the HAT Observational Study in Central and Eastern European Countries. Diabetes Ther. 2018;9(2):727-741. doi: 10.1007/s13300-018-0388-2.
59. Otto-Buczkowska E. Treatment of type 2 diabetes –what's new? Analogue insulins, and what else?. General Practitioner 2017;3(3):183-190. ISSN 2450-3517.
60. Scheen AJ, Paquot N. (Which injectable therapy after failure of oral antidiabetic agents in type 2 diabetes ?.) Rev Med Liege. 2020;75(1):60-66.
61. Oh SW, Lee JE, Shin E, Kwon H, Choe EK, Choi SY, Rhee H, Choi SH. Genome-wide association study of metabolic syndrome in Korean populations. PLoS One. 2020;15(1):e0227357.

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