



Diabetes Mellitus: Review Article

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ABSTRACT

One of the most prevalent non-communicable diseases in the world is diabetes mellitus. India faces a number of difficulties in managing diabetes, including a rising prevalence of the disease in both urban and rural areas, a lack of public awareness of the disease, a lack of adequate medical facilities, a high cost of treatment, subpar glycaemic control, and an increase in the frequency of diabetic complications. Subcutaneous injections can be used to administer insulin therapy for diabetes up to four times per day. Long-term insulin therapy has a negative impact on patient outcomes because of issues with patient compliance and the invasiveness of its administration. Type 1 diabetes is becoming more common, but type 2 diabetes mellitus, which accounts for more than 90% of all instances of diabetes, is the main cause of the epidemic. Obesity and a sedentary lifestyle are two additional risk factors for type 2 diabetes, which is a serious and prevalent chronic illness caused by a complicated interaction between genes and the environment.

Keywords: Diabetes, Medical Education, , Genetics, Genomics , Obesity

INTRODUCTION

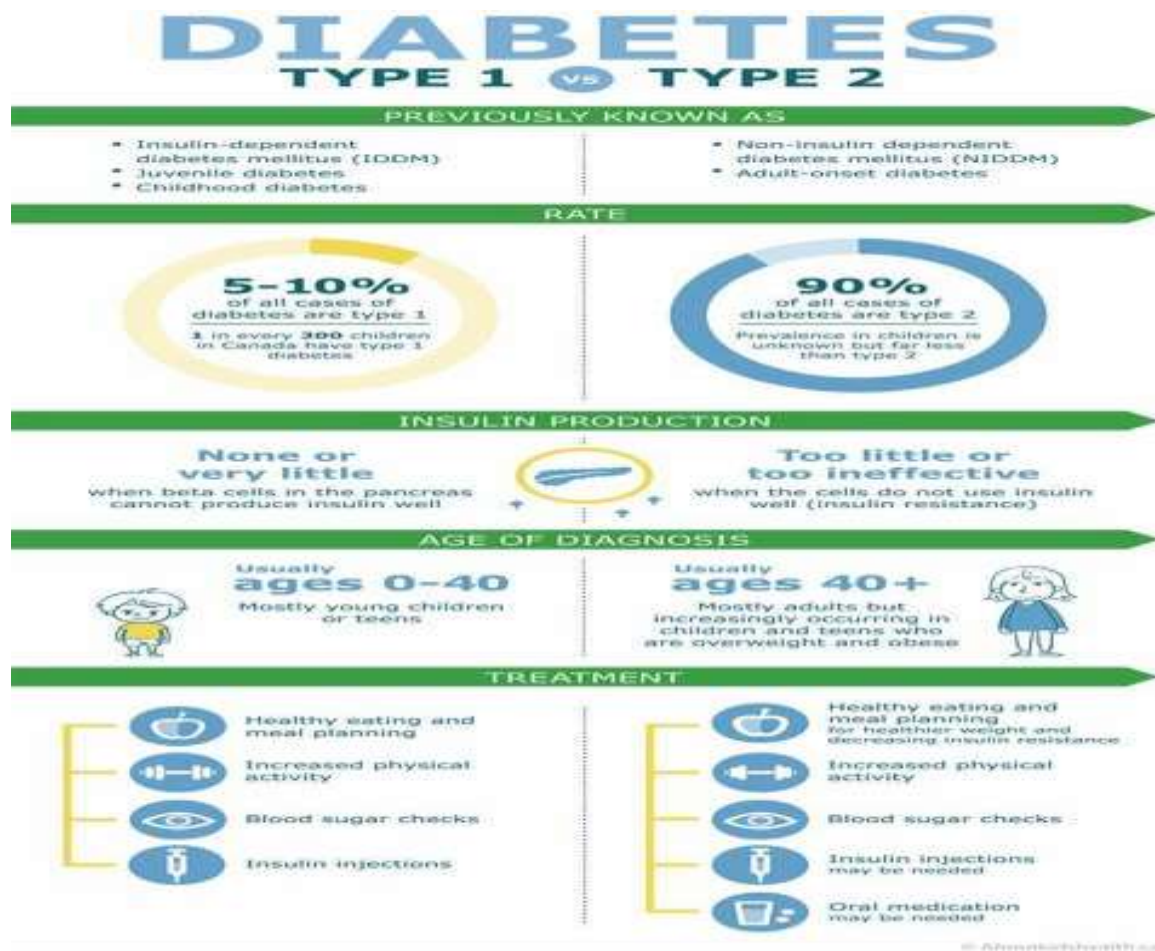
Diabetes mellitus, commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level (hyperglycemia) over a prolonged period of time. Symptoms often include frequent urination, increased thirst and increased appetite. If left untreated, diabetes can cause many health 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, damage to the nerves, damage to the eyes and cognitive impairment. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. Insulin is a hormone which is responsible for helping glucose from food get into cells to be used for energy.

Type 1 diabetes

Type 1 Diabetes results from failure of the pancreas to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" or "juvenile diabetes". The loss of beta cells is caused by an autoimmune response. The cause of this autoimmune response is unknown. Although Type 1 diabetes usually appears during childhood or adolescence, it can also develop in adults.

Type 2 diabetes

Type 2 diabetes 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" or "adult-onset diabetes". Type 2 diabetes is more common in older adults, but a significant increase in the prevalence of obesity among children has led to more cases of type 2 diabetes in younger people. 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. In women with gestational diabetes, blood sugar usually returns to normal soon after delivery. However, women who had gestational diabetes during pregnancy have a higher risk of developing type 2 diabetes later in life.

Type 1 diabetes must be managed with insulin injections. Prevention and treatment of type 2 diabetes involves maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Type 2 diabetes may be treated with oral antidiabetic medications, with or without insulin. Control of blood pressure and maintaining proper foot and eye care are important for people with the disease. Insulin and some oral medications can cause low blood sugar (hypoglycemia). Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes. Gestational diabetes usually resolves after the birth of the baby.

As of 2019, an estimated 463 million people had diabetes worldwide (8.8% of the adult population), with type 2 diabetes making up about 90% of the cases. Rates are similar in women and men. Trends suggest that rates will continue to rise. Diabetes at least doubles a person's risk of early death. In 2019, diabetes resulted in approximately 4.2 million deaths. It is the 7th leading cause of death globally. The global economic cost of diabetes-related health expenditure in 2017 was estimated at US\$727 billion. In the United States, diabetes cost nearly US\$327 billion in 2017. Average medical expenditures among people with diabetes are about 2.3 times higher.

signs and symptoms

Objective evidence of a disease such as a rash or cough is a sign. Doctors, family members, and anyone experiencing signs can identify them.

However, less noticeable disruption of normal functioning, such as abdominal pain, back pain, and malaise, is a symptom and can only be recognized by the affected individual. Symptoms are subjective. That is, others can only know the symptoms when told by the affected person.

This MNT Knowledge Center article describes the effects of signs and symptoms, and their history. The play also introduces different types of signs and symptoms, as well as their medical use.

Simple facts about signs and symptoms

Mild headaches can be a symptom because no one else can observe them. Medical symptoms are divided into chronic, recurrent, and remission symptoms. An example of a medical sign is high blood pressure that can be measured and observed by others. Anthony van Leuwenhoek invented the microscope in 1674 and changed the face of diagnostic tools.



Symptoms

There are three main types of symptoms.

Remission Symptoms:

When symptoms improve or disappear completely, they are called remission symptoms. For example, the symptoms of a cold may last for several days and then disappear without treatment.

Chronic Symptoms:

These are long-term or recurrent symptoms. Chronic symptoms are common in ongoing conditions such as diabetes, asthma, and cancer.

Recurrence Symptoms:

These are symptoms that have appeared in the past, resolved, and then returned. For example, the symptoms of depression may not appear for years, but may recur afterwards. In some cases, there are no symptoms at all. For example, a person can unknowingly suffer from high blood pressure for years, and some cancers are asymptomatic until later, more aggressive stages.

These are known as asymptomatic conditions, and the onset of symptoms is often associated with discomfort and dysfunction, but asymptomatic conditions can be fatal.

Many types of infections are asymptomatic. These are called asymptomatic infections and can be transmitted, but they do not cause any noticeable symptoms in people with the infection. The infection can be transmitted to others during the latency period or while the infectious agent has invaded the body. Another risk of asymptomatic infection is that it can cause complications that are not related to the infection itself. For example, untreated urinary tract infections (UTIs) can lead to preterm birth. Many infectious diseases, such as

HPV, are asymptomatic and can infect others. Examples of infections that initially cause no symptoms include HIV, human papillomavirus (HPV), herpes simplex virus (HSV), syphilis, hepatitis B and C. Usually talk to your doctor about another problem. It is important to have regular health checks to identify underlying problems that may not be obvious. Many cancers are asymptomatic in the early stages. Prostate cancer, for example, does not show symptoms until it has progressed to a certain point in time. This is why some cancers are so dangerous, as early treatment is often important in the treatment of cancer. For this reason, regular health checks are important for people at risk.

Sign

Medical signs are medical facts or features related to physical reactions that are confirmed by a doctor, nurse, or medical device during a patient's examination. They can often be measured, and this measurement can be central to diagnosing medical problems. Patients may be unaware of the signs and may appear irrelevant. But in the hands of doctors who know how these signs relate to other parts of the body, the same signs can hold the key to treating the underlying medical problem. ..

Some examples of signs that a doctor may be associated with a disease:

Hypertension:

This may indicate cardiovascular problems, side effects to medication, allergies, or many other possible conditions or disorders. There is sex. This is often combined with other signs to reach a diagnosis.

Fingerbeat:

This can be a sign of lung disease or many hereditary disorders. Doctors are trained to find signs that untrained people may not consider important. Signs fall into the following categories:

- **Prognostic Signs:** These are signs of the future. Instead of identifying the nature of the disease, they predict the outcome of the patient. B. What is likely to happen to him and how serious the illness is likely to be.
- **Medical History Signs:** These signs indicate part of a person's medical history. For example, skin scars may indicate a history of severe acne.

Diagnostic Signs:

These signs help doctors recognize and identify their current health problems. For example, high levels of prostate-specific antigen (PSA) in men's blood can be a sign of prostate cancer or prostate problems.

Pathological Signs:

This means that the doctor can assign the signs to the condition with absolute certainty. For example, the presence of a particular microbe in a blood sample may indicate a particular viral infection.

Diabetic emergencies

People with diabetes (usually but not exclusively in type 1 diabetes) may also experience diabetic ketoacidosis (DKA), a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. DKA requires emergency treatment in hospital.

A rarer but more dangerous condition is hyperosmolar hyperglycemic state (HHS), which is more common in type 2 diabetes and is mainly the result of dehydration caused by high blood sugars. Treatment-related low blood sugar (hypoglycemia) is common in people with type 1 and also type 2 diabetes depending on the medication being used. Most cases are mild and are not considered medical emergencies.

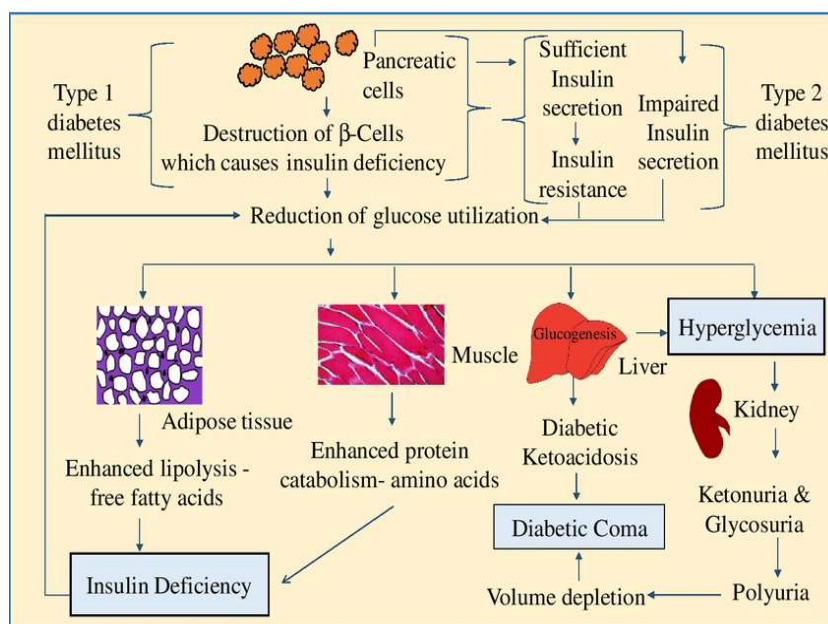
Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such as confusion, changes in behavior such as aggressiveness, seizures, unconsciousness, and rarely permanent brain damage or death in severe cases. Rapid breathing, sweating, and cold, pale skin are characteristic of low blood sugar but not definitive. Mild to moderate cases are self-treated by eating or drinking something high in rapidly absorbed carbohydrates. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon.

Pathophysiology

A patient with DM has the potential for hyperglycemia. The pathology of DM can be unclear since several factors can often contribute to the disease. Hyperglycemia alone can impair pancreatic beta-cell function and contributes to impaired insulin secretion. Consequentially, there is a vicious cycle of hyperglycemia leading to an impaired metabolic state. Blood glucose levels above 180 mg/dL are often considered hyperglycemic in this context, though because of the variety of mechanisms, there is no clear cutoff point. Patients experience osmotic diuresis due to saturation of the glucose transporters in the nephron at higher blood glucose levels. Although the effect is variable, serum glucose levels above 250 mg/dL are likely to cause symptoms of polyuria and polydipsia.

Insulin resistance is attributable to excess fatty acids and proinflammatory cytokines, which leads to impaired glucose transport and increases fat breakdown. Since there is an inadequate response or production of insulin, the body responds by inappropriately increasing glucagon, thus further contributing to hyperglycemia. While insulin resistance is a component of T2DM, the full extent of the disease results when the patient has inadequate production of insulin to compensate for their insulin resistance.

Chronic hyperglycemia also causes nonenzymatic glycation of proteins and lipids. The extent of this is measurable via the glycation hemoglobin (HbA1c) test. Glycation leads to damage in small blood vessels in the retina, kidney, and peripheral nerves. Higher glucose levels hasten the process. This damage leads to the classic diabetic complications of diabetic retinopathy, nephropathy, and neuropathy and the preventable outcomes of blindness, dialysis, and amputation, respectively.



Treatment / administration

The physiology and management of diabetes is complex and requires a variety of interventions for successful disease management. Diabetes awareness and patient involvement are important for management. Patients will get better results if they can independently monitor their diet (carbohydrates and general calorie restriction), regular exercise (more than 150 minutes a week), and blood glucose. [28]

Lifelong treatment is often required to avoid unwanted complications. Ideally, blood glucose should be maintained at 90-130 mg / dL and HbA1c should be maintained below 7%. Glucose management is important, but overly aggressive management can lead to hypoglycemia, which can have harmful or fatal consequences. Since T1DM is a disease primarily due to insulin deficiency, daily injections or insulin pump delivery is central to treatment. Diet and exercise may be appropriate treatments, especially for early-stage type 2 diabetes. Other treatments may target insulin sensitivity or increase insulin secretion by the pancreas. Specific drug subclasses include biguanide (metformin), sulfonylurea, meglitinide, α -glucosidase inhibitor, thiazolidinedione, glucagon-like peptide-1 agonist, dipeptidyl peptidase IV inhibitor (DPP-4), selective, amilinomi. Peptides, and sodium-glucose transporter-2 (SGLT-2) inhibitors. Metformin is a front-line prescription diabetes drug that works by lowering basal and postprandial plasma glucose. Insulin may also be needed for patients with type 2 diabetes, especially those with inadequate glucose management at an advanced stage of the disease. In patients with morbid obesity, obesity surgery is a possible means of normalizing blood sugar levels. Recommended for people who have failed other treatments and have serious comorbidity. [29] The GLP-1 agonists liraglutide and semaglutide correlate with improved cardiovascular outcomes. The SGLT-2 inhibitors empagliflozin and canagliflozin have been shown to not only prevent the development of heart failure, but also improve cardiovascular outcomes with potential renal protection.

Microvascular complications are a risky complication of diabetes and require regular examination. To diagnose diabetic retinopathy, qualified medical personnel should perform regular diabetic retinopathy tests. Neurological examinations using the monofilament test can identify patients with neuropathy who are at risk of amputation. Doctors may also advise patients to have a daily foot examination to identify foot lesions that may be overlooked due to neuropathy. Low-dose tricyclic antidepressants, duloxetine, anticonvulsants, topical capsaicin, and analgesics may be needed to treat neuropathic pain in diabetes. Urinary microalbumin testing can also assess early renal changes due to diabetes with albuminuria above 30 mg / g creatinine, along with an estimated GFR. The antiproteinuria effect of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) reverses the progression from microalbuminuria to macroalbuminuria in patients with delayed type 1 or type 2 diabetes. It will be the best drug for.

The FDA has approved pregabalin and duloxetine for the treatment of diabetic peripheral neuropathy. Tricyclic antidepressants and anticonvulsants have also been used to manage the pain of diabetic neuropathies, with varying successes.

ADA also recommends regular blood pressure screening for diabetics with a goal of systolic blood pressure of 130 mmHg and diastolic blood pressure of 85 mmHg. [30] Pharmacological treatment of hypertensive diabetic patients usually includes angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics, beta blockers, and / or calcium channel blockers. ADA is diabetic so that low-density lipoprotein cholesterol (LDL-C) is less than 100 mg / dL in the absence of cardiovascular disease (CVD) and less than 70 mg / dL in the case of atherosclerotic cardiovascular disease. There is a recommendation for patient lipid monitoring (ASCVD). Statins are the first-line therapy for the treatment of dyslipidemia in diabetic patients. ADA

suggests that low doses of aspirin may also be beneficial for diabetics at high risk of cardiovascular events. However, the role of aspirin in reducing cardiovascular events in diabetic patients remains unclear

Complications

Regardless of the specific type of diabetes, complications involve microvascular, macrovascular, and neuropathic issues. Microvascular and macrovascular complications vary according to the degree and the duration of poorly control diabetes and include nephropathy, retinopathy, neuropathy, and ASCVD events, especially if it is associated with other comorbidities like dyslipidemia and hypertension.[45] One of the most devastating consequences of DM is its effect on cardiovascular disease (ASCVD). Approximately two-thirds of those with DM will die from a myocardial infarction or stroke.[46] In T2DM, fasting glucose of more than 100 mg/dL significantly contributes to the risk of ASCVD, and cardiovascular risk can develop before frank hyperglycemia.[47][48]

DM is also a common cause of blindness in adults aged 20 to 74 years in the United States. Diabetic retinopathy contributes to 12000 to 24000 new cases of blindness annually, and treatments generally consist of laser surgery and glucose control.[49]

Renal disease is another significant cause of morbidity and mortality in DM patients. It is the leading contributor to end-stage renal disease (ESRD) in the United States, and many patients with ESRD will need to start dialysis or receive a kidney transplant.[49] If the albuminuria persists in the range of 30 to 300 mg/day (microalbuminuria), it seems to be a predictable earliest marker for the onset of diabetic neuropathy. When macroalbuminuria (300 mg / 24 h or more) begins, the progression to ESRD accelerates. Random spot urine samples for measuring the ratio of albumin to creatinine are the most widely used and preferred methods for detecting microalbuminuria, a rapid, easy, and predictable method. Two of the three tests performed over a 6-month period showing sustained levels of creatinine above 30 mcg / mg confirm the diagnosis of microalbuminuria.

DM is also the leading cause of limb amputation in the United States. This is primarily due to DM-related angiopathy and neuropathy. [49] Many patients who develop neuropathy require regular foot examinations to prevent infection from overlooked wounds. The duration of diabetes is the most important risk factor for the development of diabetic retinopathy. In people with type 1 diabetes, it usually develops about 5 years after the onset. Therefore, it is recommended that retinal examinations in these patients be started approximately 5 years after diagnosis. In patients with type 2 diabetes, many patients may already have retinal changes at the time of diagnosis. By the age of 10, about 10%, by the age of 15, 40%, and by the age of 20, 60% will have nonproliferative retinal disease. For these patients, it is advisable to start an annual retinal screening at the time of diagnosis. Post-study studies have shown that proper glycemic control has a positive effect on the onset and progression of diabetic retinopathy. Uncontrolled blood pressure is an additional risk factor for macular edema. Therefore, lowering blood pressure in diabetics also affects the risk of developing retinopathy.

[The most acute complication of DM is diabetic ketoacidosis (DKA), which typically presents in T1DM. This condition is usually either due to inadequate dosing, missed doses, or ongoing infection.[53] In this condition, the lack of insulin means that tissues are unable to obtain glucose from the bloodstream. Compensation for this causes the metabolism of lipids into ketones as a substitute energy source, which causes systemic acidosis, and can be calculated as a high anion-gap metabolic acidosis. The combination of hyperglycemia and ketosis causes diuresis, acidemia, and vomiting leading to dehydration and electrolyte abnormalities, which can be life-threatening. In T2DM, hyperosmolar hyperglycemic syndrome (HHS) is an emergent concern. It presents similarly to DKA with excessive thirst, elevated blood glucose, dry mouth, polyuria, tachypnea, and tachycardia. However, unlike DKA, HHS typically does not present with excessive urinary ketones since insulin still gets produced by pancreatic beta cells. Treatment for DKA or HHS involves insulin administration and aggressive intravenous hydration. Careful management of electrolytes, particularly potassium, is critical in the management of these emergent conditions.

Conclusion

Diabetes is a late murderer for whom no cure is known. However, with proper awareness and timely treatment, complications can be reduced. The three main complications are associated with blindness, kidney damage and heart attack. Strict control of a patient's blood glucose is important to avoid complications. One of the difficulties of tightly controlling blood sugar levels is that such attempts can lead to hypoglycemia. This causes far more serious complications than elevated blood sugar levels. Researchers are currently looking for alternative ways to treat diabetes. The purpose of this study is to give an overview of the current state of diabetes research. The author believes that diabetes is one of the most challenging research topics of the new century and wants to encourage new researchers to take on the challenge.]

References

- [1]. Rajaei E, Jalali MT, Shahrabi S, Asnafi AA, Pezeshki SMS, HLAs in Autoimmune Diseases: Dependable Diagnostic Biomarkers? *Current rheumatology reviews*. 2019 [PubMed PMID: 30644346]
- [2]. Klein BE, Klein R, Moss SE, Cruickshanks KJ, Parental history of diabetes in a population-based study. *Diabetes care*. 1996 Aug [PubMed PMID: 8842599]
- [3]. Barnett AH, Eff C, Leslie RD, Pyke DA, Diabetes in identical twins. A study of 200 pairs. *Diabetologia*. 1981 Feb [PubMed PMID: 7193616]
- [4]. Saxena R, Voight BF, Lyssenko V, Burt NP, de Bakker PI, Chen H, Roix JJ, Kathiresan S, Hirschhorn JN, Daly MJ, Hughes TE, Groop L, Altschuler D, Almgren P, Florez JC, Meyer J, Ardlie K, Bengtsson Boström K, Isomaa B, Lettre G, Lindblad U, Lyon HN, Melander O, Newton-Cheh C, Nilsson P, Orho-Melander M, Råstam L, Speliotes EK, Taskinen MR, Tuomi T, Guiducci C, Berglund A, Carlson J, Gianniny L, Hackett R, Hall L, Holmkvist J, Laurila E, Sjögren M, Sterner M, Surti A, Svensson M, Svensson M, Tewhey R, Blumensiel B, Parkin M, Defelice M, Barry

- R,Brodeur W,Camarata J,Chia N,Fava M,Gibbons J,Handsaker B,Healy C,Nguyen K,Gates C,Sougnéz C,Gage D,Nizzari M,Gabriel SB,Chirn GW,Ma Q,Parikh H,Richardson D,Ricke D,Purcell S, Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels. *Science (New York, N.Y.)*. 2007 Jun 1; [PubMed PMID: 17463246]
- [5]. Sladek R,Rocheleau G,Rung J,Dina C,Shen L,Serre D,Boutin P,Vincent D,Belisle A,Hadjadj S,Balkau B,Heude B,Charpentier G,Hudson TJ,Montpetit A,Pshezhetsky AV,Prentki M,Posner BI,Balding DJ,Meyre D,Polychronakos C,Froguel P, A genome-wide association study identifies novel risk loci for type 2 diabetes. *Nature*. 2007 Feb 22 [PubMed PMID: 17293876]
- [6]. Yasuda K,Miyake K,Horikawa Y,Hara K,Osawa H,Furuta H,Hirota Y,Mori H,Jonsson A,Sato Y,Yamagata K,Hinokio Y,Wang HY,Tanahashi T,Nakamura N,Oka Y,Iwasaki N,Iwamoto Y,Yamada Y,Seino Y,Maegawa H,Kashiwagi A,Takeda J,Maeda E,Shin HD,Cho YM,Park KS,Lee HK,Ng MC,Ma RC,So WY,Chan JC,Lyssenko V,Tuomi T,Nilsson P,Groop L,Kamatani N,Sekine A,Nakamura Y,Yamamoto K,Yoshida T,Tokunaga K,Itakura M,Makino H,Nanjo K,Kadowaki T,Kasuga M, Variants in KCNQ1 are associated with susceptibility to type 2 diabetes mellitus. *Nature genetics*. 2008 Sep [PubMed PMID: 18711367]
- [7]. Zeggini E,Scott LJ,Saxena R,Voight BF,Marchini JL,Hu T,de Bakker PI,Abecasis GR,Almgren P,Andersen G,Ardlie K,Boström KB,Bergman RN,Bonnycastle LL,Borch-Johnsen K,Burt NP,Chen H,Chines PS,Daly MJ,Deodhar P,Ding CJ,Doney AS,Duren WL,Elliott KS,Erdo MR,Frayling TM,Freathy RM,Gianniny L,Grallert H,Grarup N,Groves CJ,Guiducci C,Hansen T,Herder C,Hitman GA,Hughes TE,Isomaa B,Jackson AU,Jørgensen T,Kong A,Kubalanza K,Kuruville FG,Kuusisto J,Langenberg C,Lango H,Lauritzen T,Li Y,Lindgren CM,Lyssenko V,Marville AF,Meisinger C,Midhjel K,Mohlke KL,Morken MA,Morris AD,Narisu N,Nilsson P,Owen KR,Palmer CN,Payne F,Perry JR,Petersen E,Platou C,Prokopenko I,Qi L,Qin L,Rayner NW,Rees M,Roix JJ,Sandbaek A,Shields B,Sjögren M,Steinthorsdóttir V,Stringham HM,Swift AJ,Thorleifsson G,Thorsteinsdóttir U,Timpson NJ,Tuomi T,Tuomilehto J,Walker M,Watanabe RM,Weedon MN,Willer CJ,Wellcome Trust Case Control Consortium, Illig T,Hveem K,Hu FB,Laakso M,Stefansson K,Pedersen O,Wareham NJ,Barroso I,Hattersley AT,Collins FS,Groop L,McCarthy MI,Boehnke M,Altshuler D, Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. *Nature genetics*. 2008 May [PubMed PMID: 18372903]
- [8]. Fajans SS,Bell GL,Polonsky KS, Molecular mechanisms and clinical pathophysiology of maturity-onset diabetes of the young. *The New England journal of medicine*. 2001 Sep 27 [PubMed PMID: 11575290]
- [9]. Shields BM,Hicks S,Shepherd MH,Colclough K,Hattersley AT,Ellard S, Maturity-onset diabetes of the young (MODY): how many cases are we missing? *Diabetologia*. 2010 Dec [PubMed PMID: 20499044]
- [10]. Kühl C, Etiology and pathogenesis of gestational diabetes. *Diabetes care*. 1998 Aug; [PubMed PMID: 9704223]
- [11]. Felner EI,Klitz W,Ham M,Lazaro AM,Stastny P,Dupont B,White PC, Genetic interaction among three genomic regions creates distinct contributions to early- and late-onset type 1 diabetes mellitus. *Pediatric diabetes*. 2005 Dec [PubMed PMID: 16390390]
- [12]. "Diabetes Fact sheet N°312". WHO. October 2013. Archived from the original on 26 August 2013. Retrieved 25 March 2014.
- [13]. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN (July 2009). "Hyperglycemic crises in adult patients with diabetes". *Diabetes Care*. 32 (7): 1335– 1343. doi:10.2337/dc09- 9032. PMC 2699725. PMID 19564476
- [14]. Krishnasamy S, Abell TL (July 2018). "Diabetic Gastroparesis: Principles and Current Trends in Management". *Diabetes Therapy*. 9 (Suppl 1): 1– 42. doi:10.1007/s13300-018-0454-9. PMC 6028327. PMID
- [15]. Saedi E, Gheini MR, Faiz F, Arami MA (September 2016). "Diabetes mellitus and cognitive impairments". *World Journal of Diabetes*. 7 (17): 412– 422. doi:10.4239/wjd.v7.i17.412. PMC 5027005. PMID 27660 698.
- [16]. Jump up to: a b Chiang JL, Kirkman MS, Laffel LM, Peters AL (July 2014). "Type 1 diabetes through the life span: a position statement of the American Diabetes Association". *Diabetes Care*. 37 (7): 2034– 2054. doi:10.2337/dc14- 1140. PMC 5865481. PMID 24935775.
- [17]. "Causes of Diabetes". National Institute of Diabetes and Digestive and Kidney Diseases. June 2014. Archived from the original on 2 February 2016. Retrieved 10 February
- [18]. Heinrich, J., Yang, B. Y. (January 2020). "Ambient air pollution and diabetes: a systematic review and metaanalysis". *Environmental Research*. 180: 108817. Bibcode:2020ER....180j8817Y. doi:10.1016/j.envres. 2019.108817. PMID 31627156. S2CID 204787461. Retrieved 21 April 202
- [19]. Ripsin CM, Kang H, Urban RJ "Management of blood glucose in type 2 diabetes mellitus" (PDF). *American Family Physician*. 79 (1): 29– 36. PMID 19145963. Archived (PDF) from the original on 2013-05-05
- [20]. Brutsaert EF (February 2017). "Drug Treatment of Diabetes Mellitus". *MSDManuals.com*. Retrieved 12 October 2018.
- [21]. "IDF DIABETES ATLAS Ninth Edition 2019" (PDF). www.diabetesatlas.org. Retrieved 18 May 2020. 11. "About