Episode 93 – Diabetes – Part 2: Diagnosis & Management

September 22, 2023

Introduction

Diabetes is a group of metabolic disorders characterized by elevated blood glucose levels. Diabetes is associated with several significant clinical complications, including retinopathy, nephropathy, cardiovascular disease,[1] neuropathy, and poor wound healing.

Diabetes is suggested by the typical symptoms of hyperglycemia (e.g., polydipsia, polyphagia, polyuria)[2] and is diagnosed by measuring blood glucose levels. Diabetes may be suspected in individuals who have frequent bacterial and fungal infections and foot ulcers. Diabetes is often detected through screening tests on individuals who are at risk of diabetes but are asymptomatic. [1] [2]

Screening for diabetes

Blood glucose levels are often screened during routine medical examinations, especially in older individuals, since diabetes is common in later life. Routine tests to screen for type 1 diabetes are not usually done, even in those at high risk of type 1 (e.g., siblings or children of individuals with type 1 diabetes). However, screening individuals at risk of type 2 diabetes[3] is important because they may unknowingly have diabetes. [1] [2]

Diabetes diagnosis

Diabetes and prediabetes are diagnosed through blood tests that measure glucose, including A1C, fasting plasma glucose, random plasma glucose, oral glucose tolerance, and glucose challenge tests. [2] [3] [4]

Diagnostic blood tests [3] [4]

Test	Description
A1C test (also called hemoglobin A1C [HbA1C], glycated hemoglobin, or	Measures glycosylation of the hemoglobin molecule (i.e., percentage of hemoglobin A that has glucose attached) providing an estimate of the average levels of blood glucose over the last 3 months. Reported as the percentage of hemoglobin that is glycosylated.

[1] Refer to Episodes 79, 80, and 81 for discussion on cardiovascular disease.
[2] Refer to Episode 91 for additional signs and symptoms of diabetes.
[3] Risk factors for type 2 diabetes include prediabetes, overweight, age >40 years, family history of type 2 diabetes, sedentary lifestyle, unhealthy eating, and HIV infection. Refer to Episode 91 for additional risk factors.

Test	Description
glycosylated hemoglobin tests)	Fasting not required.
Fasting plasma glucose test	Measures blood glucose level at a single point in time. Fasting for at least 8 hours required.
Random plasma glucose test	Used when there are symptoms of diabetes. Fasting not required.
Oral glucose tolerance test	Used to diagnose prediabetes, type 2 diabetes, and gestational diabetes. Fasting for at least 8 hours required. Blood sample taken to measure glucose level after fasting, then a liquid high in glucose is consumed. Another blood sample is taken two hours later to measure blood glucose level. For pregnant individuals, blood is drawn every hour for two to three hours. Gestational diabetes may be indicated if blood glucose levels are high two or more times during the test.
Glucose challenge test (also called glucose screening test)	Tests for gestational diabetes. Sample of blood taken one hour after drinking a liquid high in glucose. Fasting not required. An oral glucose test while fasting may be required if blood glucose level is high.

Test results for diagnosing prediabetes and diabetes [5] [6] [7] [8]

Diagnosis	A1C	Fasting plasma glucose test	Random plasma glucose test	Oral glucose tolerance test*
Normal	4.0 – 5.9%	≤6.0 mmol/L**	N/A	<7.8 mmol/L
Prediabetes	6.0 – 6.4%	6.1 – 6.9 mmol/L	N/A	7.8 – 11.0 mmol/L
Diabetes	≥6.5%	≥7.0 mmol/L	≥11.1 mmol/L	≥11.1 mmol/L

*2 hours after 75 grams glucose intake.
**Glucose levels <2.2 mmol/L in females or <2.8 mmol/L in males may require further investigation.
Two tests are used to confirm the diagnosis of diabetes.

Urine glucose measurement, once commonly used, is no longer used for monitoring or diagnosing diabetes because it is neither sensitive nor specific. Urine testing can be misleading because the amount of glucose in the urine may not reflect the current level of glucose in the blood. Blood glucose levels can become very low or reasonably high without any change in glucose levels in the urine. [1] [2]

If diabetes is diagnosed, further tests can be conducted to determine if the individual has type 1 diabetes. For example, blood can be tested for autoantibodies (e.g., islet cell or glutamic acid decarboxylase autoantibodies) that are often present in type 1 diabetes but not in type 2 diabetes. However, the absence of autoantibodies does not rule out type 1 diabetes. Urine may be tested for ketones (byproducts from the breakdown of fat), which also indicates type 1 diabetes instead of type 2 diabetes. [5] [9] [10]

Monitoring diabetes treatment

Monitoring blood glucose levels is essential in diabetes care. Routine blood glucose monitoring provides the information needed to make necessary adjustments in

medications, diet, and exercise regimens. Glycemic control can be monitored by measuring blood levels of:
a) Glucose
b) A1C
c) Fructosamine [1] [2]

a) Glucose
Glucose levels are typically determined by home monitoring capillary blood glucose or continuous glucose monitoring. Individuals with diabetes need to monitor their blood glucose levels to ensure they remain within their target range to help to prevent severe hypoglycemia or hyperglycemia.

Capillary blood glucose (also called self-monitored blood glucose) determines glucose in the capillary blood using a fingerstick and a glucose meter. Timing and frequency of capillary blood glucose is individualized and based on several factors,[4] including:
- Type of diabetes
- Type of antihyperglycemic therapy
- Changes to antihyperglycemic therapy
- Whether glycemic targets are being met
- Propensity to hypoglycemia
- Awareness of hypoglycemia
- Literacy and numeracy skills
- Occupation requires strict avoidance of hypoglycemia
- Acute illness [11] [12]

Continuous glucose monitoring (also called real-time continuous glucose monitoring) utilizes a wearable continuous glucose monitor that measures interstitial fluid glucose every few minutes, throughout the day and night. This monitoring is vital for individuals who experience low blood glucose at night (i.e., nocturnal hypoglycemia) and risk not waking up in the morning. The readings are relayed in real time to a device which can be read by the individual, caregiver, or healthcare provider, even remotely. A continuous glucose monitor includes a small disposable sensor that is worn under the skin (often on the stomach or arm). The sensor sends the glucose levels to an attached transmitter and, usually, to a separate receiving device, such as a smart phone.

Many continuous glucose monitors work with apps with features such as:
- Ability to track food and beverage consumption, physical activity levels, and the medications taken.
- Ability to download data onto a computer or smart device to monitor glucose level trends.
- An alarm that goes off when glucose level is too low or too high, helping prevent emergencies. [13] [14] [15]

[4] Self-monitoring Blood Glucose Tool is an interactive tool to help individuals with diabetes determine how often to check their blood glucose levels. https://guidelines.diabetes.ca/self-management/smbg-tool-pwd

Integrated continuous glucose monitor (also called a closed-loop insulin-delivery system or an artificial pancreas) uses a continuous glucose monitor, an insulin pump, and software to allow the two to communicate. This system automatically adjusts insulin delivery based on continuous glucose monitor readings. [13]

Flash glucose monitoring (also called intermittently scanned continuous glucose monitoring) uses an externally worn glucose sensor with a small filament inserted under the skin of the upper arm to measure interstitial fluid glucose (e.g., FreeStyle Libre). When the sensor is "flashed" or scanned with a separate touchscreen reader device, it transmits the real-time glucose reading and information on the most recent 8-hour trend to the reader. If the individual performs at least three sensor scans per day at approximately 8-hour intervals, the flash glucose monitor can record 24-hour glucose profiles. A sensor can be worn continuously for up to 14 days. [14] [16]

Professional continuous glucose monitoring (also called masked continuous glucose monitoring) measures interstitial fluid glucose via a sensing device that stores the data to be retrieved at a later time. It is a diagnostic tool for use by diabetes care providers, not for diabetes self-management. [14]

Recommended blood glucose targets for most individuals with diabetes* [17]

	A1C	Fasting blood glucose / blood glucose before meals (preprandial)	Blood glucose two hours after eating (postprandial)
Target for most individuals with diabetes	≤7.0%	4.0 – 7.0 mmol/L	5.0 – 10.0 mmol/L (5.0 – 8.0 mmol/L if A1C targets not being met)

*Targets are different for pregnant individuals, older adults, and children ≤12 years.

Factors affecting blood glucose

Factors that can cause blood glucose levels to change include:

- Diet (e.g., foods high in carbohydrates raise glucose levels).
- Exercise (may decrease blood glucose levels).
- Stress (tends to increase blood glucose levels).
- Infection (tends to increase blood glucose levels).
- Medications (a number of drugs are associated with hyperglycemia including corticosteroids, some thiazide diuretics, beta-blockers, antipsychotics, etc. Non-diabetes drugs associated with hypoglycemia include alcohol, some beta-blockers, angiotensin-converting enzyme [ACE] inhibitors, etc.).
- Time of day (e.g., dawn phenomenon and Somogyi effect).[5] [2] [18] [19]

[5] Dawn phenomenon refers to periodic episodes of hyperglycemia in the early morning hours because of the normal release of hormones (e.g., cortisol and growth hormone) which signals the liver to boost production of glucose to help individuals wake up. However, individuals with diabetes may not produce enough insulin or are insulin resistant to counter the increase in blood glucose elevating blood glucose levels upon wakening. [59] [60]
Somogyi effect is rebound hyperglycemia in the morning after an episode of hypoglycemia overnight, often induced by excess insulin or inadequate calorie intake with insulin therapy before bed. Somogyi effect is the body's response to hypoglycemia during the night. To compensate, the body raises the blood glucose too high in the morning. [59]

b) A1C
For most individuals with diabetes, A1C should be measured approximately every three months to ensure glycemic goals are being met or maintained. A1C is check more frequently in some circumstances, (e.g., significant changes made to therapy, during pregnancy). Testing at least every six months should be performed in adults with consistently good control. It is potentially harmful to wait until there are symptoms of hypoglycemia or hyperglycemia to check blood glucose.

Certain conditions can falsely elevate, decrease, or produce normal A1C values:

- False elevations of A1C may occur with low red blood cell turnover (e.g., in iron, folate, or vitamin B12 deficiency anemia), high-dose aspirin, and high blood alcohol concentrations.
- False normal A1C values may occur with increased red blood cell turnover, as occurs with hemolytic anemias and hemoglobinopathies (e.g., sickle cell anemia, thalassemia), or during treatment of deficiency anemias.
- False decreased A1C values may occur with pregnancy, cirrhosis, or chronic kidney disease (stages 4 and 5). [1] [11]

c) Fructosamine
Fructosamine is an amino acid that has bonded with glucose (mainly glycosylated albumin) and reflects glucose control in the previous one to two weeks. It is used when A1C results are not reliable, such as in anemia caused by iron, folate, or vitamin B12 deficiency, or abnormal forms of hemoglobin (e.g., sickle cell disease, thalassemia), which cause false A1C results. However, it is mainly used in research settings. [1] [2]

Diabetes treatment
The goal of diabetes treatment is hyperglycemia control to relieve symptoms and prevent complications, while minimizing hypoglycemic episodes. General treatment of diabetes includes:

a) Healthy diet
b) Physical activity
c) Education
d) Weight loss for individuals who are overweight
e) Medication
f) Appropriate monitoring and control of blood glucose levels to prevent diabetes complications [20]

Kianmehr et al. (2022) showed controlling type 2 diabetes can add years to an individual's life. The study focused on four measures commonly used to monitor diabetes: A1C; body mass index (BMI); blood pressure; and low-density lipoprotein cholesterol (LDL-C). They found better control of these biomarkers can potentially increase the life expectancy by three years in an average individual with type 2 diabetes. For individuals with very high levels of A1C, systolic blood pressure, LDL-C, and BMI, controlling biomarkers could potentially increase life expectancy by more than ten years. Life span can also be extended even if individuals do not hit their optimal treatment goals. Generally, more modest improvement extends life, albeit to a lesser

extent. The researchers hope to show individuals with type 2 diabetes the benefits of controlling their disease. [21]

a) Healthy diet

Diet management is essential and should focus on a healthy, balanced diet to help maintain a healthy weight. Individualized dietary recommendations should be based on the individual's tastes, preferences, culture, and goals, and should accommodate requirements posed by comorbid conditions. Dietary education includes consuming a diet rich in whole foods rather than processed foods. Carbohydrates should be high quality and contain adequate amounts of fibre, vitamins, and minerals, and be low in added sugar, fat, and sodium. Individuals with diabetes and caregivers who prepare their meals should receive nutrition counselling with a registered dietitian. Individuals taking insulin should avoid long periods between meals to prevent hypoglycemia. [1] [2]

Many ultra-processed foods and beverages contain added sugars.[6] Overconsumption of added sugars can contribute to oral conditions (e.g., caries[7] and periodontal disease[8]), and is associated with increase risk of developing systemic conditions, including type 2 diabetes and cardiovascular disease. [22] [23]

b) Physical activity

Exercise, at least 150 minutes of moderate- to vigorous-intensity aerobic exercise a week (e.g., 30 minutes, 5 days/week), can help with weight control and improve blood glucose levels. Aerobic exercise and resistance training have been shown to improve glycemic control in type 2 diabetes. Several studies have shown a combination of resistance and aerobic exercise to be superior to either alone. Exercise has been shown to decrease mortality and improve A1C in type 1 diabetes.

Individuals must be alert for symptoms of hypoglycemia since blood glucose levels decrease during exercise. Some individuals need to eat a small snack during prolonged exercise, decrease their insulin dose, or both.

Some individuals may have difficulty adding exercise to their daily routine, particularly if they have not been active in the past or if they have a disorder that limits their movement (e.g., arthritis). However, they may be able to add exercise to their usual routine (e.g., walking instead of driving, climbing stairs instead of taking the elevator). Activity goals may need to be modified for individuals with diabetes complications (e.g., neuropathy, retinopathy). [1] [2] [24]

c) Education

Education is crucial to optimize diabetes care and should include information on:

- Causes of diabetes
- Diet
- Physical activity

[6] Refer to Episode 86 for a list of hidden sources of sugars in food.
[7] Refer to Episodes 86 and 87 for discussion on dental caries.
[8] Refer to Episodes 5, 6, 9, 22, 31, 37, 42, 47, 49, and 50 for information on periodontal disease.

- Medication
- Self-monitoring with fingerstick testing or continuous glucose monitoring
- A1C
- Signs and symptoms of hypoglycemia, hyperglycemia, and diabetes complications
- Oral health[9]

Formal diabetes self-management education programs, generally conducted by diabetes nurses and registered dieticians, are often very effective and have been shown to improve diabetes outcomes. Regular oral healthcare appointments are important to help individuals with diabetes manage their disease.[9] [1] [25]

d) Weight loss

Weight loss is important for individuals who are overweight. Approximately, 80-90% of individuals with type 2 diabetes are overweight or obese. Some individuals with type 2 diabetes may be able to avoid or delay drug therapy by achieving and maintaining a healthy weight. Weight loss is also important because excess weight contributes to diabetes complications.[10] When individuals who are obese have trouble losing weight with diet and exercise alone, weight-loss medication may be prescribed (e.g., Orlistat). Certain diabetes medications can induce weight loss, especially, glucagon-like peptide 1 (GLP-1), such as Ozempic; and sodium-glucose cotransporter-2 (SGLT2) inhibitor medications (e.g., Invokana, Jardiance). [2]

Bariatric surgery may be considered in individuals with type 2 diabetes with an:

- Inability to achieve or maintain weight loss, despite repeated attempts with different therapies; and
- BMI of ≥35.0.

Bariatric surgery can result in sustained weight loss and improved control or remission of type 2 diabetes. Bariatric surgery in Ontario is publicly funded for those who meet eligibility criteria. [26]

Marquezin et al. (2022) highlighted the significant decline in oral health among individuals with morbid obesity undergoing or preparing for bariatric surgery. The study involved 100 participants divided into those receiving dietary counselling and those undergoing gastroplasty. Questionnaires, oral examinations, saliva samples, and cheek swabs were analyzed for dietary changes, weight loss, inflammatory markers, oral microbiota, and oral health, before and three and six months after surgery or the start of the diet. Participants were asked to floss and brush their teeth three times a day. The findings revealed a deterioration in oral health, marked by increased caries, gingivitis, and periodontitis, in both groups, but particularly those who underwent bariatric surgery.

Salivary markers showed impaired acid buffering capacity, essential for maintaining pH and preventing tooth demineralization. Bacterial genome sequencing showed

[9] Refer to Episode 94 for discussion on oral health and diabetes.
[10] Refer to Episode 91 for information on complications associated with diabetes.

alterations of microbiota diversity, especially in the gastroplasty group, with an increase in periodontal pathogens.

The diet of many participants improved, but profound dietary changes were believed to be the main cause of oral health deterioration, especially because more frequent meals were not accompanied by more frequent oral self-care, and more food was liquid or puréed in the first few months after surgery, increasing food and biofilm accumulation. The research emphasizes the vital role of oral health clinicians in the care of individuals undergoing bariatric surgery. [27]

e) Medication

There are many medications used to treat diabetes. All individuals with type 1 diabetes require insulin[11] to lower blood glucose levels and will become ketoacidotic[12] without it (build up of ketones in the blood from the body breaking down fat as fuel). Most individuals with type 2 diabetes require oral medications but some also require insulin or other injectable medications. [2]

Insulin

Insulin preparations are primarily produced by recombinant DNA technology and are formulated either as structurally identical to human insulin or as a modification of human insulin (insulin analogues). Human insulin and insulin analogues are preferred and used by most adults with type 1 diabetes. However, preparations of animal-sourced insulin are still accessible in Canada although rarely required. Inhaled insulin is currently not approved for use in Canada but has received FDA approval and is available in the US under the brand name Afrezza. [28]

Insulin types are commonly categorized by their time to onset and duration of action. Insulin is available in four basic forms:

- Rapid-acting insulin reaches maximum activity in about 1 hour and works for 3 to 5 hours. Rapid-acting insulins are injected at the beginning of a meal.
- Short-acting insulin (e.g., regular insulin) begins acting slightly more slowly and lasts longer than rapid-acting insulin. Regular insulin reaches its maximum activity in 2 to 4 hours and works for 6 to 8 hours. It is injected 30 minutes before eating a meal.
- Intermediate-acting insulin starts to work within 0.5 to 2 hours, reaches its maximum activity in 4 to 12 hours, and works for 13 to 26 hours depending on which type is used. This type of insulin may be used in the morning to provide coverage for the first part of the day or in the evening to provide coverage during the night.
- Long-acting insulin has very little effect during the first few hours but provides coverage for 20 to 40 hours depending on which type is used.

[11] Pancreatic islets, also called islets of Langerhans, are groups of cells in the pancreas. The normal human pancreas contains about one million islets. Islets contain several types of cells, including beta cells that make the hormone insulin. Insulin controls the amount of glucose in the blood. Glucose in the bloodstream stimulates the pancreas to produce insulin. Insulin helps glucose to move from the blood into the cells. Once inside the cells, glucose is converted to energy, which is used immediately, or the glucose is stored as fat or glycogen until it is needed. [2] [58]

[12] Refer to Episode 91 for additional information on ketoacidosis.

- Combinations of insulin are commercially available in premixed preparations. Premixed insulin starts to work in 15 to 60 minutes and can last from 10 to 16 hours. The peak time varies depending on which insulins are mixed. [29] [30]

Types of insulin [31] [32]

	Basal insulin	Prandial (bolus) insulin	Premixed insulin
Description	Intermediate- or long-acting insulin, usually injected once daily (usually at bedtime) and used to keep blood glucose levels stable during periods of fasting (e.g., between meals, while sleeping).	Short- or rapid-acting insulin injected at mealtime to control post-meal (post-prandial) glucose levels or for short-term correction of meal-related hyperglycemia.	Premixed solutions that contain two types of insulin (e.g., prandial and basal insulin).
Indications	First-line treatment for insulin-naive individuals. Simpler treatment regimen that causes less hypoglycemia and weight gain compared to premixed insulin or prandial-only regimens.	May be added at mealtimes if glycemic control is suboptimal after 3-6 months on basal insulin (with other agents). Basal and prandial (bolus) insulin may be started together if blood glucose level is high (≥16.7 mmol/L) and metabolic decompensation is present at initial diagnosis. Evidence of metabolic decompensation includes marked hyperglycemia, ketosis or unintentional weight loss.	Used for individuals who cannot accommodate >2 injections/day (e.g., they require caregiver support to administer insulin, or have difficulty adjusting insulin doses [e.g., due to cognitive ability or visual acuity]). Less flexible dosing option (requires a routine mealtime to prevent hypoglycemia) and offers less ability to correct for abnormal results.

Insulin administration

Insulin is injected subcutaneously into the fat layer (e.g., in arm, thigh, abdomen)[13] via:

- Small syringes with very thin needles. Syringes must be loaded.
- Insulin pen which contains a cartridge that holds the insulin.
- Insulin pump (also called continuous subcutaneous insulin infusion) pumps insulin continuously from a reservoir through a small cannula left in the skin. Administration rate can be adjusted depending on the time of day, whether the individual is exercising, or other factors. Additional doses can be released as needed for meals or to correct hyperglycemia.
- Integrated continuous glucose monitor. [29]

Complications of insulin treatment

Hypoglycemia is the most common complication of insulin treatment when blood glucose is generally <4.0 mmol/L. Hypoglycemia occurs more often in individuals who try to strictly control blood glucose levels.

[13] If insulin is delivered intramuscularly, its uptake and action become variably faster, leading to suboptimal, inconsistent glucose control. [61]

Symptoms of mild or moderate hypoglycemia include headache, diaphoresis (excess sweating), palpitations, light-headedness, blurred vision, nausea, agitation, weakness, confusion, and difficulty concentrating or speaking.

Symptoms of severe hypoglycemia include seizures and loss of consciousness. In older adults, hypoglycemia may cause stroke-like symptoms of aphasia or hemiparesis and is more likely to precipitate stroke, myocardial infarction, and sudden death. Individuals who have frequent hypoglycemia may be unaware of hypoglycemic episodes because they no longer experience symptoms (i.e., hypoglycemia unawareness). [20] [29]

Since individuals with hypoglycemia may be too confused to recognize their blood glucose is too low, it is important for members of their household, trusted others, and healthcare providers to be familiar with signs of hypoglycemia.

Causes of hypoglycemia include:
- More physical activity than usual
- Eating less than usual
- Not eating on time
- Taking too much diabetes medication
- Drinking alcohol [33]

Nocturnal hypoglycemia
Blood glucose levels can drop during sleep, stay low for several hours, and can cause serious complications (e.g., seizures, coma, cardiovascular events). Symptoms of nocturnal hypoglycemia can include:
- Restlessness, crying out, talking, or having nightmares
- Night sweats causing bed linens or pajamas to be damp
- Waking up feeling tired, irritable, confused, or having a headache

However, nocturnal hypoglycemia is often asymptomatic and goes unrecognized. It can interfere with sleep, quality of life, mood, and ability to work. Having hypoglycemia during sleep can also make the individual less likely to notice and respond to symptoms of hypoglycemia during the day.

It is important to note if the individual experiencing nocturnal hypoglycemia can be woken and sit without support, they should be given a fast-acting glucose source. However, glucagon is used when the individual is unable to swallow oral glucose because of severe hypoglycemia symptoms, including extreme drowsiness, unconsciousness, or seizure.

Glucagon
Glucagon is a hormone that helps the liver release glucose to raise blood glucose levels. Glucagon can be administered through:
- Injection (e.g., GlucaGen HypoKit delivered intramuscularly; Glucagon delivered subcutaneously, intramuscularly, or intravenously)
- Nasal spray (e.g., Baqsimi) [34] [35] [36]

To prevent relapse of hypoglycemia, oral carbohydrates should be given to restore the liver glycogen when the individual has responded to the glucagon treatment. If the individual does not respond within ten minutes after glucagon administration, medical attention should be sought immediately; intravenous (IV) glucose must be administered as soon as an IV access can be established.

Glucagon is designed to be administered in emergency situations to the individual by relative(s), friends, coworkers, etc. It is imperative that others (especially caregivers of children with type 1 diabetes) know where it is kept and how to use it. [37] [38] [39]

Reducing risk of medical emergencies in oral healthcare

In general, to reduce the risk of hypoglycemia, clients with diabetes should be scheduled for morning appointments when glucose levels tend to be highest. A morning appointment after a normal breakfast is usually best for clients on insulin therapy. Clients should be advised to eat normally and take their usual medications, unless their primary medical provider recommends that they change their dose or medication prior to oral healthcare treatment.

Postpone routine oral healthcare if the diabetes is poorly controlled, until blood glucose is better controlled. If treatment is urgent (e.g., pain, swelling), consult with the primary medical provider about having treatment in a hospital or special setting where the client can be monitored during and after surgery.

Severe hypoglycemia in oral healthcare constitutes a medical emergency and prompt emergency treatment is required. All clients with symptomatic hypoglycemia, even if corrected during the appointment, should be referred for prompt medical attention.

Diabetic ketoacidosis is a potentially life-threatening condition (more common in type 1 than in type 2 diabetes). If diabetic ketoacidosis is suspected, all procedures should be stopped, and emergency medical services should be contacted immediately.

Signs and symptoms of diabetic ketoacidosis include fruity (acetone) breath, excessive thirst, frequent urination, nausea, vomiting, fatigue, dry skin and mucous membranes, flushed facial appearance, abdominal tenderness, confusion, and deep, rapid breathing.

To reduce the risk of hyperglycemia and ketoacidosis, treatment and wait time should be minimized to decrease client stress. Appropriate pain management during procedures should also be utilized. Stressful situations cause the release of hormones that can affect insulin uptake and blood glucose levels.

Oral healthcare practices must have a medical emergency action plan and an up-to-date emergency kit, including a fast-acting source of glucose. The emergency action plan needs to be posted in convenient locations throughout the office. All office staff should be aware of this plan and the procedures to follow should a medical emergency arise. The plan should be reviewed at staff meetings so everyone understands their roles and responsibilities during a medical emergency. [40] [41] [42] [43] [44]

Fast-acting glucose source
Symptoms of hypoglycemia usually respond rapidly to ingestion of sugar. Fast-acting glucose sources (containing 15 grams) include:

- 15 g of glucose in the form of glucose tablets (preferred choice)
- 15 mL (1 tablespoon) or 3 packets of table sugar dissolved in water
- 5 cubes of sugar
- 150 mL (2/3 cup) of juice or regular soft drink
- 6 LifeSavers® (1 = 2.5 g of carbohydrate)
- 15 mL (1 tablespoon) of honey (do not use for children less than one year) [20] [33]

Other complications of insulin treatment include:

- Hyperglycemia as a result of conditions such as dawn phenomenon and Somogyi effect.
- Local allergic reaction, which occurs rarely and causes pain and burning, followed by redness, itchiness, and swelling around the injection site for several hours.
- Generalized allergic reaction. Very rarely, anaphylactic reaction may occur after injected insulin.
- Local fat atrophy or hypertrophy is a common reaction which can make the skin look lumpy or indented. Although this reaction is not an allergic reaction, it can decrease insulin absorption and action. It is important to systematically rotate injection sites to help avoid these problems.
- Insulin antibodies. In very rare cases, the body produces antibodies to injected insulin. These antibodies may interfere with insulin's activity, requiring very large doses. [20] [29]

Pancreas transplantation
Sometimes individuals with type 1 diabetes receive transplantation of an entire pancreas or only the islet cells from a donor pancreas as an alternative to insulin therapy. This procedure can result in insulin independence and may improve glycemic control and prevent severe hypoglycemia, but there are risks from long-term immunosuppression.

Possible side effects of immunosuppressants include:

- Increased risk of infections
- Increased risk of developing cancer
- Gastrointestinal problems (e.g., vomiting, nausea, diarrhea)
- Headaches, tremors, or confusion
- Hypertension
- Hyperglycemia
- High cholesterol and triglyceride levels
- Kidney damage

Transplantation is usually done only in individuals who have serious complications due to diabetes or who are receiving kidney transplantation for end stage renal disease and will require immunosuppressants anyway.

Islet allotransplantation involves the infusion of islets isolated from a deceased donor pancreas via the portal vein into the liver. The islet cells lodge in the small blood vessels of the liver, where they can live and produce insulin. Sometimes two or three infusions are done, requiring two or three deceased donors. On average, about 400,000 islets are transplanted in each procedure. Immunosuppressants are needed to help reduce the risk of rejection. Transplanting islet cells is simpler and safer than pancreas transplantation, and about 75% of individuals who receive an islet cell transplant no longer need insulin one year after transplantation and may not need it for many more years. However, the long-term success of islet cell transplantation is not yet proved.

Pancreas transplantation can result in complete independence from insulin therapy in the majority of individuals. However, post-transplant diabetes is common after solid organ transplantation and is associated with increased risk for mortality, cardiovascular disease, and graft loss. The limited number of specialized islet and pancreas transplantation centres and the relatively small number of donor pancreases limit the availability of these treatments. [2] [45] [46] [47] [48]

Type 2 diabetes

Type 2 diabetes is often initially treated with diet and exercise. If glycemic control is not achieved, oral, injectable, or a combination of these medications may be prescribed. Medications prescribed for type 2 diabetes include:

- Biguanide
- Dipeptidyl peptidase 4 (DPP-4) inhibitors
- Glucagon-like peptide-1 (GLP-1) receptor agonists
- Sodium-glucose co-transporters type 2 (SGLT2) inhibitors
- Alpha-glucosidase inhibitors
- Sulfonylureas
- Meglitinides
- Thiazolidinediones
- Insulin [20]

Type 2 diabetes medications [32] [49]

Class	Name* Generic (brand name)	Mechanism of action	Considerations*	Side effects*
First-line glucose-lowering medication				
Biguanide	Metformin (Glucophage) Metformin extended-release (Glumetza)	Enhances insulin sensitivity in liver and peripheral tissues so insulin is used more effectively Other medications may be added if metformin and healthy behaviour changes do not control blood glucose level	First-line drug due to its safety, low cost, and possible heart benefits Reduction in myocardial infarction in individuals who are overweight Low risk of hypoglycemia No weight gain Contraindications include chronic kidney disease stage 4 and 5 and hepatic failure	Nausea and diarrhea (usually resolves within 1-2 weeks) Headache Vitamin B12 deficiency
Second-line glucose-lowering medications				
DPP-4 inhibitors	Alogliptin (Nesina) Linagliptin (Trajenta) Saxagliptin (Onglyza) Sitagliptin (Januvia)	Increases insulin levels after meals Inhibits glucagon release (a hormone that raises blood glucose) Slows digestion, reduces appetite	No weight gain Low risk of hypoglycemia Caution with saxagliptin in heart failure	Rare pancreatitis Rare severe joint pain
GLP-1 receptor agonists	*Short-acting* Exenatide (Byetta) Lixisenatide (Adlyxin) *Longer-acting* Semaglutide (Ozempic) Dulaglutide (Trulicity) Exenatide extended-release (Bydureon) Liraglutide (Victoza)	Injectable medications Increases insulin levels after meals Inhibits glucagon release Slows digestion, reduces appetite	Requires subcutaneous injection Low risk of hypoglycemia Reduced progression of nephropathy with liraglutide Contraindicated with personal/family history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2	Nausea, vomiting, diarrhea (usually resolves with time) Associated with weight loss Rare cases of acute gallstone disease

Class	Name* Generic (brand name)	Mechanism of action	Considerations*	Side effects*
SGLT2 inhibitors	Canagliflozin (Invokana) Dapagliflozin (Forxiga) Empagliflozin (Jardiance)	Inhibits SGLT-2 transport protein, which prevents kidneys from reabsorbing sugar. Extra glucose is eliminated through the urine	Low risk of hypoglycemia Reduced progression of nephropathy and reduction in heart failure in participants with clinical cardiovascular disease with empagliflozin and canagliflozin Caution with renal dysfunction, loop diuretics in the elderly Dapagliflozin contraindicated with bladder cancer	Genital yeast infections Urinary tract infections Increased urination Increased thirst Hypotension Associated with weight loss Small increase in LDL-C Rare cases of diabetic ketoacidosis (which may occur without hyperglycemia) Increased risk of fractures and amputations with canagliflozin
Alpha-glucosidase inhibitors	Acarbose (Glucobay)	Inhibits pancreatic α-amylase and intestinal α-glucosidase	No weight gain Requires 3 times daily dosing	Gastrointestinal side effects, such as stomach pain, gas, diarrhea
Sulfonylureas	Gliclazide (Diamicron) Gliclazide modified-release (Diamicron MR) Glimepiride (Amaryl) Glyburide (Diabeta) [chlorpropamide and tolbutamide are still available in Canada, but rarely used]	Helps pancreas release more insulin	Gliclazide preferred over glyburide due to lower risk of hypoglycemia, cardiovascular events, mortality Relatively rapid blood glucose-lowering response	Hypoglycemia Weight gain
Meglitinides	Repaglinide (GlucoNorm)	Helps pancreas release more insulin	Relatively rapid blood glucose-lowering response Requires 3-4 times daily dosing	Hypoglycemia Weight gain
Thiazolidinediones	Pioglitazone (Actos) Rosiglitazone (Avandia)	Enhances insulin sensitivity in peripheral tissues and liver	6-12 weeks required for maximum effect	Weight gain Mild increase in HDL-C Increased risk of heart failure, edema, and fractures

Class	Name* Generic (brand name)	Mechanism of action	Considerations*	Side effects*
				Rare bladder cancer (pioglitazone) Cardiovascular controversy (rosiglitazone)
Insulin	<u>Bolus (prandial) insulins</u> *Rapid-acting analogues* Aspart Aspart (faster-acting) Glulisine Lispro U-100 Lispro U-200 *Short-acting* Regular <u>Basal insulins</u> *Intermediate-acting* NPH *Long-acting analogues* Degludec U-100 Degludec U-200 Detemir Glargine U-100 Glargine U-100 (biosimilar) Glargine U-300 <u>Premixed insulins</u> Premixed regular-NPH Biphasic insulin aspart	Activates insulin receptors to regulate metabolism of carbohydrate, fat, and protein	Requires subcutaneous injection Potentially greatest A1C reduction No maximum dose Numerous formulations and delivery systems allows for flexible regimens May be used at diagnosis with marked hyperglycemia Can be used temporarily during illness, stress, pregnancy, or for a medical procedure or surgery	Weight gain Risk of hypoglycemia

Class	Name* Generic (brand name)	Mechanism of action	Considerations*	Side effects*
	Lispro/lispro protamine suspension			
Weight loss agent				
Gastrointestinal lipase inhibitor	Orlistat (Xenical)	Promotes weight loss by inhibiting lipase, which blocks absorption of ~30% of fat consumed Undigested fat is passed in stool	Used in combination with diabetes medication (sulfonylureas, metformin and/or insulin) to improve blood glucose control Used in individuals who are overweight or obese with type 2 diabetes, who do not respond adequately to diet, exercise and diabetes medicines alone Requires 3 times daily dosing Does not suppress appetite Contraindications include: chronic malabsorption syndrome, cholestasis, pregnancy, breastfeeding,	Diarrhea and other gastrointestinal side effects Risk of hypoglycemia Reduced absorption of some fat-soluble vitamins and beta-carotene (vitamin supplementation usually advised to ensure adequate nutrition)

*Nonexhaustive list

Other medications

Other medications are often prescribed to prevent diabetes complications, such as:

- Angiotensin-converting enzyme [ACE] inhibitors or angiotensin II receptor blockers [ARBs]) for those with hypertension or chronic kidney disease.
- Statins for those ≥40 years to decrease the risk of cardiovascular disease.
- Aspirin for those with risk factors for cardiovascular disease. [20] [29]

Repurposing metformin

Metformin has been identified as a potential COVID-19[14] therapeutic agent because of its antiviral activity in vitro and its anti-inflammatory and antithrombotic activities. Data from observational studies have suggested individuals receiving metformin as treatment for their diabetes at the time of their COVID-19 diagnosis had a lower risk of progressing to severe COVID-19. However, metformin is not recommended for COVID-19 treatment in nonhospitalized or hospitalized individuals, except in clinical trials. [50]

Older age and certain health conditions (e.g., overweight, obesity) can increase the risk of developing long COVID.[15] Thus, finding treatments to reduce risk of the condition is valuable. Bramante et al. (2023) assessed the effect of metformin on risk of developing long COVID. Participants were between ages 30 and 85 and overweight or obese. The results showed outpatient treatment with metformin reduced long COVID incidence by ~41%. More research is required to determine whether metformin helps prevent long COVID in individuals who have been vaccinated against COVID-19 or who previously had COVID-19. It is important to note research suggests individuals who are vaccinated against COVID-19 are less likely to develop long COVID. [51] [52]

Metformin is also being investigated for the prevention of oral cancer in individuals with oral leukoplakia or erythroplakia. Dr. Leigha Rock[16] is leading the three-year chemotherapy prevention trial at Dalhousie with colleagues in the U.S. and Canada. Estimated completion date of this study is July 2026. [53] [54]

Research by Dandona et al. (2023) showed promising results using semaglutide (e.g., Ozempic) to treat individuals with type 1 diabetes. Most individuals with new-onset type 1 diabetes have substantial intact beta-cell reserve. Accordingly, the researchers analyzed the efficacy of semaglutide in individuals with a new diagnosis of type 1 diabetes. Ten adults initially received a 0.125-mg dose of weekly semaglutide, which was adjusted up to a maximum of 0.5 mg per week as prandial insulin was adjusted down. Within three months of starting semaglutide, all participants were completely off prandial insulin. Within 6 months, seven participants were also able to eliminate basal insulin. These preliminary observations support the need for prospective, randomized clinical trials with larger numbers of participants to investigate this approach further. [55]

[14] Refer to Episodes 10, 13, 27, 28, 31, 33, 34, 52, 59, and 71 for information on COVID-19.
[15] Refer to Episodes 28, 38, 48, and 71 for information on long COVID (post COVID-19 condition).
[16] Refer to Episode 64 for the interview with Dr. Rock on research she led on COVID-19 and dental hygienists.

Type 2 diabetes remission

Remission of type 2 diabetes (i.e., achieving A1C in non-diabetes range after stopping glucose-lowering medications) is possible for some individuals. Remission is not a cure, but reflects the often temporary resolution of hyperglycemia and subsequent possible relapse with progression of type 2 diabetes.

Achieving remission is more likely for individuals:

- Diagnosed with type 2 diabetes for a shorter time (e.g., <6 years);
- With overweight or obesity, who are able and inclined to lose weight;
- With blood glucose levels that are not too elevated; and
- Who do not take insulin.

Careful assessment must be given to individuals living with eating and/or mental health disorders, and concurrent medical conditions should be addressed when considering remission of type 2 diabetes.

Stopping certain glucose-lowering medication(s) with proven benefits on reducing heart and/or kidney disease complications may not be recommended for individuals with type 2 diabetes who have a history of cardiovascular disease and/or kidney disease.

Sustained weight loss of ≥15 kg (~33lbs) of initial body weight is associated with the greatest probability of type 2 diabetes remission.

There are currently three therapeutic approaches which have demonstrated type 2 diabetes remission: bariatric surgery, a low-calorie (~800-850 kcal/day) total dietary/meal replacement diet, and a structured exercise program combined with a calorie-restricted diet.

A medical provider or diabetes care team can help determine if type 2 diabetes remission is appropriate. If so, they will help select the best therapeutic option among the available strategies to give the individual the best chance of remission, and make appropriate referrals. [56] [57]

Take home messages

- It is important for oral health practitioners to update medical histories prior to treatment to determine clients' diabetes medications, compliance with diabetes therapy, and glycemic control (e.g., A1C and most recent glucose level via capillary blood glucose or continuous glucose monitoring) to facilitate safe care and help prevent medical emergencies.
- Oral health practitioners should be aware of the symptoms of hypoglycemia and hyperglycemia and be able to identify at-risk clients.
- Consultation and/or referral to an appropriate medical practitioner as required (e.g., uncontrolled blood glucose, evidence of diabetes complications).
- Individuals with uncontrolled diabetes are at increased risk of medical emergencies, including severe hypoglycemia, severe hyperglycemia (i.e., diabetic ketoacidosis and hyperosmolar hyperglycemic state), coma, myocardial infarction, and stroke.

- Oral health practitioners must be prepared to recognize and respond to medical emergencies using appropriate emergency equipment and medications when necessary.

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Client Resources

Self-monitoring Blood Glucose Tool
An interactive tool to help individuals with diabetes determine how often to check their blood glucose levels. https://guidelines.diabetes.ca/self-management/smbg-tool-pwd

Remission Possible
Provides information for individuals who want to learn more about putting type 2 diabetes into remission. https://www.diabetesremission.ca/

Additional Resources

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