Diabetes Type 2: Nothing Sweet About It (174)

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Contact hours: 7

Course price: $39

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Course Summary

Overview of type 2 diabetes, including underlying physiology, clinical forms, prevalence, causes, and complications. Addresses prediabetes and metabolic syndrome, as well as the normal regulation of blood glucose levels and insulin production/resistance. Explores complex management issues.

COI Support

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No commercial support was received for this activity.

Criteria for Successful Completions

80% or higher on the post test, a completed evaluation form, and payment where required. No partial credit will be awarded.

Course Objectives

When you finish this course you will be able to:

- Summarize the history of Diabetes Mellitus.
- Summarize the prevalence, mortality, and morbidity of diabetes.
- Compare and contrast the four classifications of diabetes mellitus.
- Explain the body's regulation of blood glucose during the normal metabolism of foods and the pathology that arises with diabetes mellitus.
- Describe risk factors for diabetes mellitus.
- Explain the diagnostic criteria for diabetes mellitus.
- Identify risk factors for metabolic syndrome and prediabetes.
- Describe the optimal diabetes healthcare team and how they teach self-management.
- Explain treatment strategies for diabetes.
- Compare and contrast the acute and chronic complications of type 2 diabetes.
- Discuss the chronic complications of type 2 diabetes.
- Explain the two prongs of type 2 diabetes prevention.

T2DM: A "Sweet" Walk Through Time

Samuel Gonzalez, an obese 58-year-old Hispanic man presents to his primary care provider (PCP) feeling constantly tired and sleepy. When questioned, he complains he is drinking more soda than usual because he feels thirsty all the time and also reports blurred vision and decreased sensation in his feet. As a construction worker, he wants to feel better so he can do his job.

What additional questions should be asked about Samuel's symptoms? What lab tests would you expect to be ordered to evaluate his problems? What diagnosis would you expect?

On brief history alone, could you have identified classic risk factors for diabetes mellitus? What diagnostic criteria would confirm your suspicions? Once the diagnosis of type 2 diabetes mellitus (T2DM) is confirmed, what are the next steps in helping Samuel manage his chronic condition? At the completion of this course, you will be able to guide Samuel, and countless others with T2DM, to better health.

In the first five minutes that you are reading this course, two people will die of diabetes-related causes and fourteen adults will be newly diagnosed (CDC, 2014). T2DM is the seventh leading cause of death in the United States (the number one cause is cardiovascular disease). More than 29.1 million people have been diagnosed with diabetes mellitus (CDC, 2014). That's about 1 in every 10 Americans. The disease has become a new epidemic in our country; however, it is not a new disease.

* * *

Diabetes mellitus is an ancient disease, the clinical symptoms of which were identified by the ancient Egyptians more than 3000 years ago (Ebbell, 1937). The Greek word *diabetes* means "to siphon through" and describes polyuria (excess urination), which is a classic symptom of hyperglycemia. Centuries after diabetes was recognized, the term *mellitus*, which means "sweet honey," was added to describe the sweet urine identified with chronic hyperglycemia (Ahmed, 2002).

For centuries there was no known reversal of symptoms for diabetes. Treatment strategies varied from starvation to overfeeding, bleeding, and even riding horseback to stop the polyuria. During the opium trade, patients were treated with opium (known as "doping"), which didn't cure the disease—but the patients probably didn't care! None of these treatments cured diabetes because for centuries the cause for the sweet and high volume of urine was unknown.

Then in 1673 a German scientist removed a pancreas from a dog and induced diabetes mellitus, creating the same symptoms of excessive thirst and polyuria. Nearly two centuries later unique pancreatic cells were identified as the source of sugar problems in the blood and urine. The juicy substance of the pancreas, distinct from the exocrine juices, was named **insulin** (Latin for "island") in 1916 (Pratt, 1954).

*Islets of Langerhans: Insulin-producing cells in the pancreas, discovered by and named for the scientist Paul Langerhans (1847–1888).

Once the lack of insulin was identified as the cause for diabetes mellitus, several scientists worked to extract, refine, and administer the substance. A German scientist, Georg Zuelzer (1870–1949), successfully injected the pancreatic extract into eight patients with diabetes; however, his research was halted due to demands that he work on weaponry for World War I. Similarly, a Romanian physician, Nicolas Paulescu (1869–1931), injected the pancreatic solution into the jugular veins of diabetic dogs, reversing symptoms, but his research was halted by the same world war (Pratt, 1954).

A continent away from European researchers, Canadians Frederick Banting (1891–1941) and Charles Best (1899–1965) isolated the insulin molecule and received credit for the discovery of insulin in 1921 (Pratt, 1954). They successfully filed a patent and contracted with Eli Lilly, a pharmaceutical company, to manufacture the newfound "medication."

Scientists and physicians then began to understand the relationship between insulin and sugar in the bloodstream. Insulin was identified as an anabolic hormone, which builds the body and allows nutrients that are eaten to enter the body cells for growth and life. So, over many millennia and through the contributions of numerous physicians and scientists, we finally understand the powerful connection between sugar and insulin.

Sugar comes from the carbohydrates we eat and it requires insulin in order to move from the blood into the cells of the body and be used as energy. Without insulin, or minimally sufficient amounts, sugar remains in the bloodstream causing hyperglycemia, which is the hallmark symptom of diabetes mellitus (DM). Hyperglycemia causes high blood **osmolarity** (concentration of particles), which pulls water from tissues in an attempt to dilute the blood, causing polyuria and dehydration. The dehydration in turn causes polydipsia (excessive thirst) and the cycle of excess urination and dehydration continues.

Without the needed energy from glucose the cells may starve, and the individual may lose weight as the body breaks down fat and protein for alternate sources of energy. The resulting classic triple signs of diabetes are shown in the box below.

Classic Triple Signs of Diabetes

- Polyuria (excessive urination)
- Polydipsia (excessive thirst)
- Polyphagia (extreme hunger)

Walking through time together to learn about the millennia-old disease of diabetes mellitus helps us to appreciate how far we have come in understanding this growing epidemic.

Test Your Knowledge

The symptoms of diabetes mellitus were first identified:

A. in 1921 by Canadian scientists Banting and Best.

B. by European physicians around World War I.

C. by early Egyptians and Ayurvedic healers over 3000 years ago.

D. by the American Diabetes Association in 1960.

Apply Your Knowledge

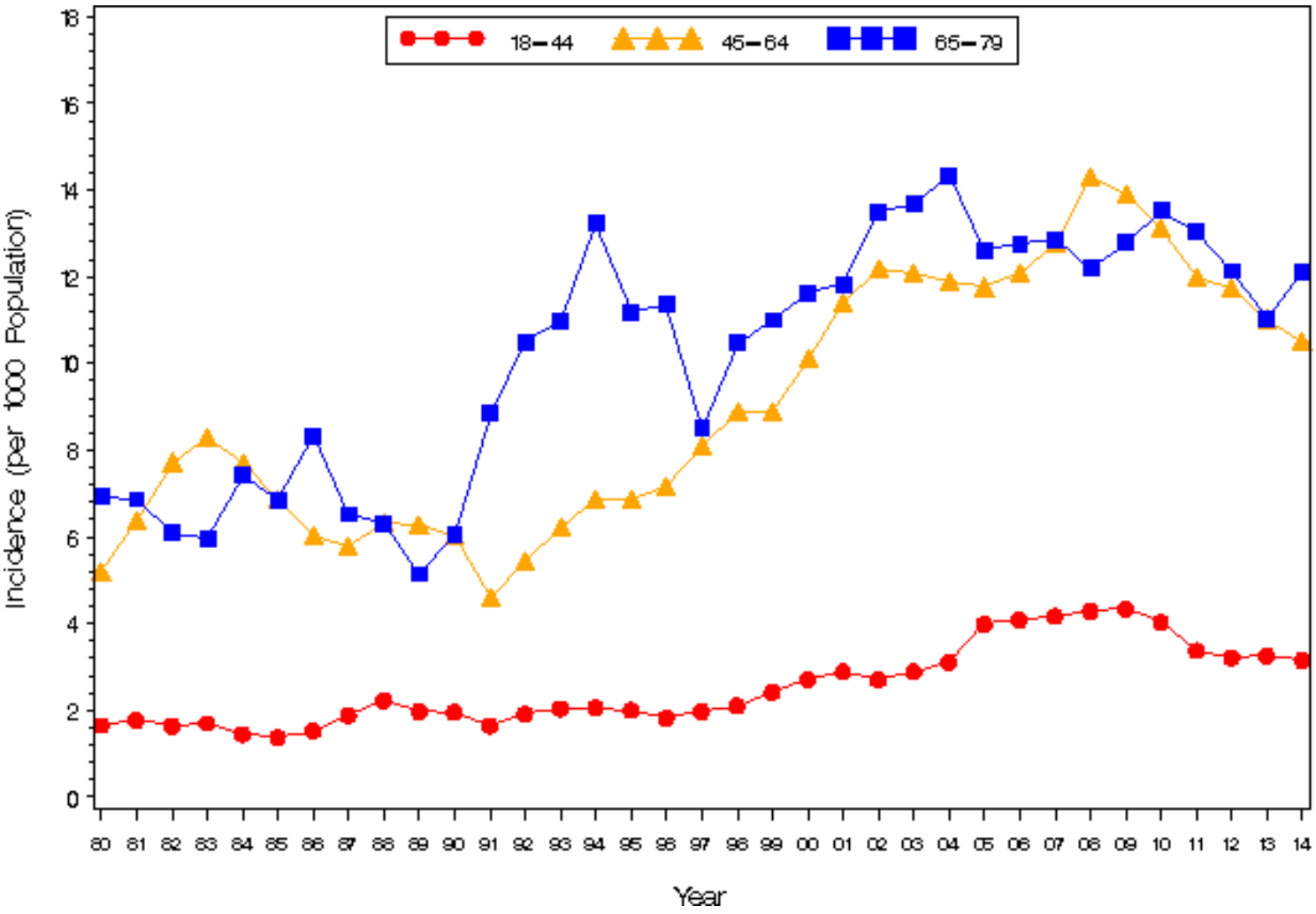
How does knowing about the history of diabetes improve your understanding of the disease and its treatment?

Answer: C

The Scope of Diabetes

Unfortunately, diabetes has become a common disease in the United States and worldwide. About 9% of Americans have DM, and 90% to 95% of them have type 2 diabetes (ADA, 2015). Americans living in poverty are more likely to have diabetes than middle-class and affluent Americans. Diabetes has also been correlated with obesity, creating a new term among healthcare professionals called "diabesity." Alarmingly the trend is increasing each decade in our country, with a higher incidence of both diabetes and obesity that is projected to worsen. With current trends of obesity and metabolic syndrome, by the year 2030, 1 in every 3 people will develop diabetes mellitus (Wild et al., 2004).

Percentage of U.S. Population with Diagnosed Diabetes, 1980–2014



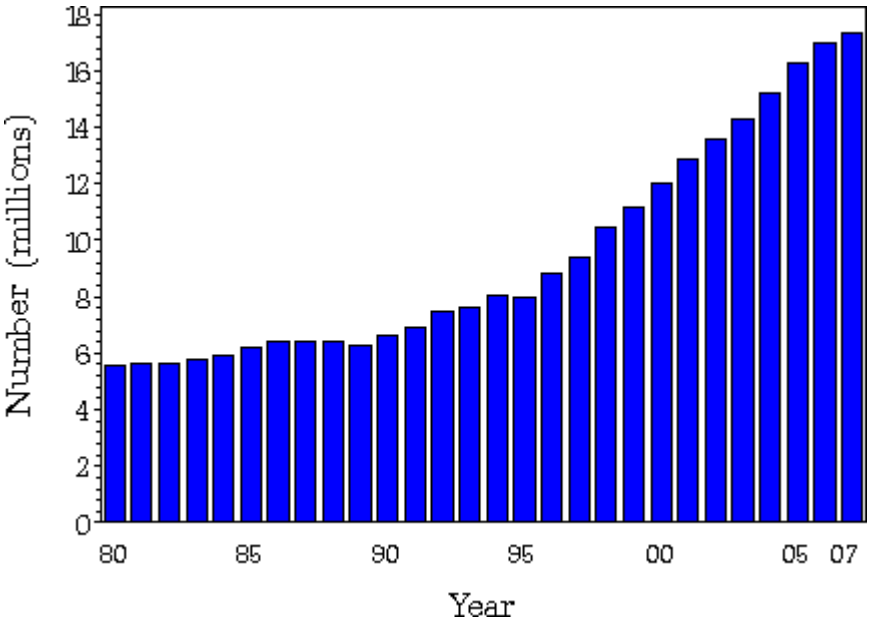
Source: CDC, 2015.

As shown in the above graph, from 1980 through 2014 the percentage of the civilian, non-institutionalized population with diagnosed diabetes mellitus increased by:

- 200% (from 0.6% to 1.8%) for those aged 0–44 years
- 124% (from 5.5% to 12.3%) for those aged 45–64 years
- 127% (9.1% to 20.7%) for those aged 65–74 years
- 126% (8.9% to 20.1%) for those aged 75 years and older

In general, the percentage of people with diagnosed diabetes has increased among all age groups. In 2014 the percentage of diagnosed diabetes among people aged 65 to 74 (20.7%) was more than 11 times that of people younger than age 45 (1.8%). It has been said 80% of people older than age 75 will eventually develop DM due to pancreatic fatigue and the prevalence of obesity. The number of Americans with diagnosed diabetes has more than tripled from 5.5 million in 1980 to 22 million (CDC, 2014). Looked at pragmatically, that becomes job security for you as a healthcare professional!

Prevalence of Diabetes by Year

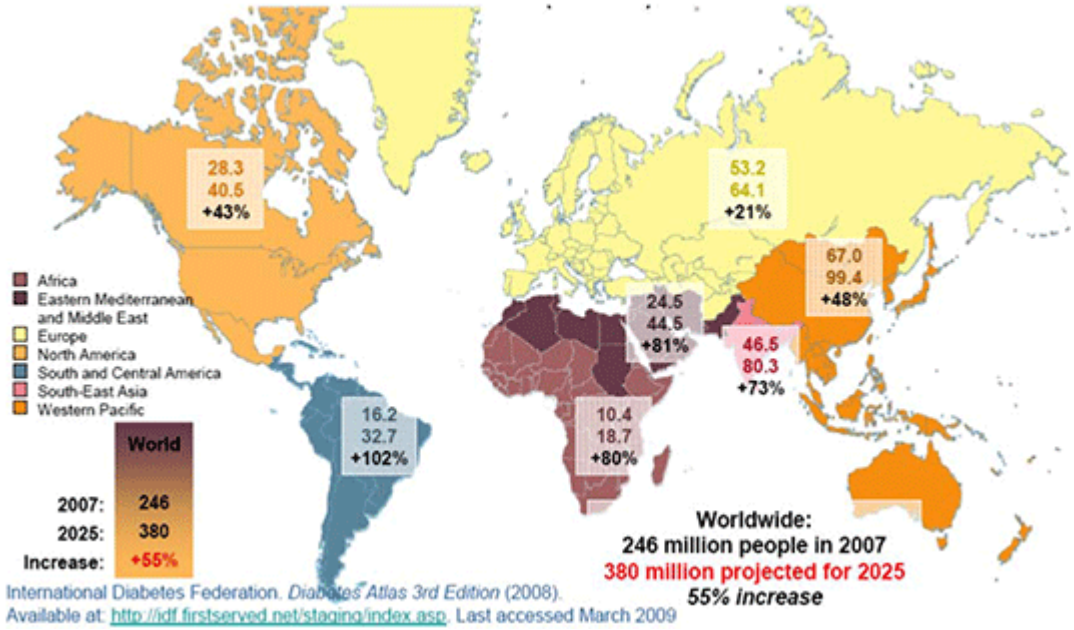


Source: Advanced Adrenal Education, 2011.

Worldwide Prevalence of T2DM

Diabetes is increasing dramatically throughout the world. As countries become industrialized, with less manual labor, their populations become more sedentary and people eat a higher calorie Western diet, which fosters the development of type 2 diabetes. More than 3% of the world's population has been diagnosed with diabetes, with the highest concentrations in developed countries.

Prevalence of T2DM Across the World



International Diabetes Federation. *Diabetes Atlas 3rd Edition* (2008). Available at: http://idf.firstserved.net/staging/index.asp. Last accessed March 2009

Prediabetes and Metabolic Syndrome

Due to the burden of rising numbers of people with DM, more attention has been directed at preventing the disease. In efforts to screen for diabetes, millions more individuals are being identified as having **prediabetes**, which presents as higher-than-normal blood sugar levels—but not quite high enough to diagnose as diabetes mellitus. A normal fasting blood sugar is 60 to 100 mg/dL. Diabetes is diagnosed by a fasting blood sugar >125 mg/dL. Prediabetes, or impaired fasting glucose, is diagnosed by a fasting blood glucose >100 mg/dL and <126 mg/dL. The prevalence rose dramatically from 27% in 2000 to 34% by 2010 (Abraham & Fox, 2013). It is estimated that 19% of Americans currently have prediabetes, which is 86 million Americans age 20 and older, and up from 79 million in 2010 (ADA, 2014).

Picture yourself in a room of 100 people: 19 people will have prediabetes, 8 of them will have type 2 diabetes, 1 will have type 1 diabetes and another 34 will have metabolic syndrome, which is another risk factor that will be discussed later in this course (Aguilar et al., 2015).

The Cost of Diabetes

Generally when we speak of the cost of anything, we are referring to economic cost. The costs of diabetes, however, are not only financial but also in terms of morbidity and mortality.

Economic Cost

Diabetes mellitus is an expensive disease. The total estimated cost of diabetes mellitus in the United States in 2012 was $245 billion. Direct medical costs were $176 billion, which includes doctor visits, surgeries, hospitalizations, prescription medications to treat complications, inpatient nursing stays, and medical supplies. An additional $69 billion is estimated for loss in productivity, sick days, early retirement due to illness, and other factors (ADA, 2012).

The majority (62%) of the costs are paid by government insurance programs such as Medicare, Medicaid, and the military, which means taxpayers are paying the bill. Those without insurance have 55% more emergency department (ED) visits, increasing the overall cost of problems that may have been preventable with adequate medical care and health coaching. The trend is moving toward increased economic costs; the medical expenses in 2012 were 41% higher than 2007, which was $174 billion. The human cost, however is even more. Loss of enjoyable quality of life and relationships may be the more tragic costs.

Mortality (Death)

Diabetes is listed as a contributor to 10% of American deaths. This makes diabetes the seventh leading cause of death listed on U.S. death certificates. Although cardiovascular disease is listed as the number one cause of death, people with diabetes mellitus are at 4 to 6 times greater risk for cardiovascular disease, still placing diabetes as a top cause of premature death. Overall, the risk for death among people with diabetes is twice that of people of similar age without diabetes (NIDDK, 2008). Adults with diabetes have a 59% higher risk for death than nondiabetics.

Morbidity (Illness)

A person with diabetes is more likely to be hospitalized than is a person without diabetes. The hospital stay is likely to be longer due to complications (Moghissi et al., 2009). Diabetes hospitalizations are largely due to the other major health problems caused or worsened by diabetes (NIDDK, 2008). Chronic hyperglycemia is the primary metabolic problem of T2DM. Persistent excess glucose in the blood damages tissues throughout the body. People with long-standing type 2 diabetes can have cardiovascular damage, kidney destruction, retinal damage, peripheral nerve damage, foot problems, poor wound healing, and an increased risk of developing Alzheimer's disease. These problems generally begin years before diabetes is even diagnosed.

For example:

- **Heart disease.** People with diabetes are 2 to 4 times more likely to die of heart disease than people without diabetes.
- **Stroke.** People with diabetes are 2 to 4 times more likely to have a stroke than people without diabetes.
- **High blood pressure.** Three out of four people with diabetes have hypertension.
- **Eye damage.** In the United States, diabetes is the leading cause of adult blindness.
- **Kidney disease.** In the United States, diabetes is the leading cause of kidney failure.
- **Nerve damage.** 60% to 70% of people with diabetes have nerve damage, known as *neuropathy*.
- **Amputations.** In the United States, the majority of nontraumatic leg or foot amputations is in people with diabetes.
- **Dental disease.** One out of three people with severe periodontal disease have diabetes.

By identifying diabetes early, many chronic complications can be avoided or minimized. For example, cardiovascular and microvascular complications may be prevented or delayed when glycemic levels are controlled. A hallmark study known as the Diabetes Control and Complications Trial (DCCT) revealed maintaining blood glucose levels to a near-normal level may significantly reduce chronic complications. The DCCT demonstrated in 1993 that microvascular complications could be reduced up to 70% when glycemic goals are within near-normal levels.

Test Your Knowledge

What percentage of Americans have diabetes mellitus?

A. 50% of adults
B. 35% of adults, or over 86 million people
C. 1 in 100
D. 9% of adults, or over 29 million people

Apply Your Knowledge

What can you do to make an impact on the high statistics of diabetes?

Answer: D

Classification of Diabetes Mellitus

The classification of diabetes mellitus includes Type 1, Type 2, and gestational diabetes, plus a catchall known simply as "other."

Clinical Definition of DM

Diabetes is defined by the American Diabetes Association as "a group of disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels" (ADA, 2015).

Diabetes is a disorder that causes chronically high concentrations of sugar (blood glucose) in the bloodstream. This chronic hyperglycemia gradually produces tissue damage, especially to eyes, kidneys, nerves, heart, and both large (macro) and small (micro) blood vessels. To simplify the definition for patients, you could say that in diabetes the body doesn't use food effectively. Although the hallmark symptom of diabetes is hyperglycemia, as noted above there are four different classes or types of diabetes based on the different pathologies involved.

Scenarios

Several patients may present with similar symptoms but be diagnosed with different types of diabetes mellitus. See if you can determine what type of diabetes each patient has.

Patient 1

An 8-year-old Caucasian girl presents with polyuria, polydipsia, weight loss, and fatigue for two months.

Patient 2

A 57-year-old obese African American man presents with polyuria, polydipsia, weight loss, and fatigue for two months.

Patient 3

A 28-year-old overweight pregnant Hispanic woman presents with polyuria, polydipsia, and fatigue for two months.

Patient 4

A 15 year-old Caucasian girl presents with polyuria, polydipsia, and fatigue for 2 months.

* * *

Each one of these patients presents with very similar symptoms and all result in a diagnosis of DM, yet each has a different pathology and can be diagnosed with a different type of diabetes.

Patient 1 has type 1 diabetes mellitus, and labs would probably reveal the patient has **insulinopenia**, or absence of endogenous insulin, generally due to an autoimmune response that resulted in destruction of insulin-producing beta cells. This patient would require insulin injections for the rest of her life.

Patient 2 has developed type 2 diabetes with risk factors of age, ethnicity, and obesity. This patient will need strategies for weight loss, meal planning, and probable combinations of antihyperglycemic medications for the rest of his life if lifestyle behavior change is not enough to control hyperglycemia.

Patient 3 has gestational diabetes, possibly with risk factors of ethnicity and overweight. This patient will probably require insulin injections for the duration of the pregnancy. Generally, after delivery the hyperglycemia will resolve. This patient may be at risk to later develop type 2 diabetes if she remains overweight or obese after the pregnancy.

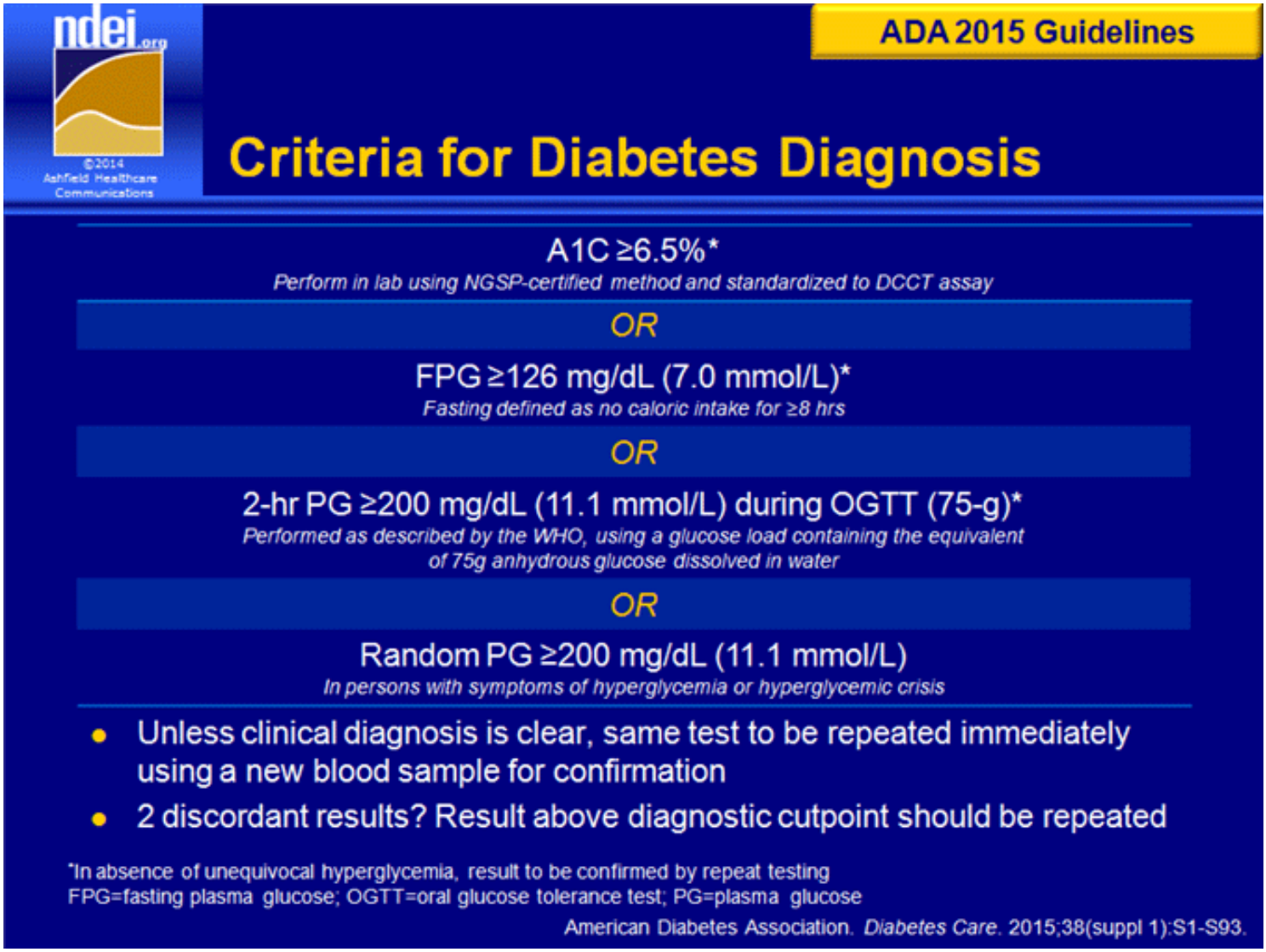
Patient 4 has the "other" class of diabetes, which includes mature onset diabetes of the young (MODY), and is a genetic predisposition to insulin resistance. The "other" category also includes latent autoimmune diabetes of the adult (LADA) and other endocrinopathies such as polycystic ovarian syndrome. This patient may or may not require insulin injections but will generally be able to control hyperglycemia with oral antihyperglycemics and balancing movement and meals.

* * *

Knowing the diagnostic criteria is essential to identify who qualifies as having DM and what is the best treatment strategy to control hyperglycemia. The ADA 2015 criteria approved four tests, which include:

- FPG >125 mg/dl on two different days. FPG is the fasting plasma glucose, the blood concentration of glucose after >8 hours of no caloric intake.
- A random blood glucose concentration >200 mg/dl with symptoms of chronic hyperglycemia (polyuria, polydipsia, and unexplained weight loss)
- OGTT >200 mg/dl on two different days. OGTT is an oral glucose-tolerance test, the measurement of a person's blood glucose level 2 hours after drinking 75 g of anhydrous glucose dissolved in water.
- A1C of 6.5% or higher (ADA, 2015)

Hyperglycemia on only one of the four tests is sufficient for a diagnosis of DM. Additional tests may be ordered to confirm the difference between type 1 and type 2 and include a C-peptide (which measures how much insulin the body can produce), auto-antibody studies (which reveal an autoimmune response seen in type 1 and LADA) and genetic studies (which may reveal a genetic disorder as in MODY).



Categories of DM

There are four major categories of diabetes: type 1, type 2, gestational, and "other."

Type 1 Diabetes

Type 1 diabetes, or T1DM, is characterized by insufficient insulin secretion. Type 1 diabetes usually results from autoimmune destruction of the beta cells in the pancreas. People with type 1 diabetes need **exogenous** (sources outside the body) **insulin** to survive. People with type 1 diabetes represent only 5% to 10% of all people with diabetes (Maitra, 2009). People with type 1 diabetes cannot make sufficient insulin to survive.

In the past, type 1 diabetes was called "insulin-dependent diabetes." The ADA changed the nomenclature as more patients with type 2 became dependent on insulin for sugar regulation, which was confusing to both patients and healthcare providers; so the name reverted back to "type 1."

Type 1 diabetes has also been called *juvenile diabetes* because it typically appears in children and young adults. Type 1 diabetes can present as an acute illness; however, the destruction of the beta cells may have been occurring for weeks prior to the acute symptoms.

Type 2 Diabetes

Type 2 diabetes, or T2DM, is the most common form of diabetes, and is characterized by insulin resistance, or sluggish response of insulin after food consumption. Type 2 diabetes represents 90% of all people with diabetes. **Insulin resistance** is the reduced response of skeletal muscle cells to take up insulin. Type 2 diabetes is characterized by two main defects: insulin resistance, in which many cells in the body become less responsive to insulin; and beta cell deterioration, which leads to sluggish production of insulin by the pancreas.

Even before the disease shows clinical signs and symptoms, mildly elevated blood glucose (BG) levels can be detected in tests. This stage of the disease is called **prediabetes**. The progression of type 2 diabetes is gradual. Over the years, the individual's prediabetes worsens, especially if the person is overweight and inactive.

Type 2 diabetes was once called "adult-onset diabetes" because the disease develops slowly and typically appears in older adults. Ninety to ninety-five percent of all present cases of diabetes are type 2; however, the age at which the condition is being diagnosed continues to lower, even including obese children. In the United States, type 2 diabetes is found in less than 2.5% of people aged 20 to 39 years, 10.5 % of people aged 40 to 59 years, and 23% of people 60 years of age or older.

Type 2 diabetes mellitus is a progressive disease that inevitably worsens over time, even with appropriate management and maintenance of the therapeutic regimen. For many individuals, up to 50% of beta cell function is lost by the time the diagnosis is made. An additional 3% to 5% may be lost in each subsequent year (UK Prospective Diabetes Study Group, 1998). People with type 2 diabetes also have a progressively reduced secretion of insulin. Initially, many people with type 2 diabetes can live without additional insulin; however, the disease worsens, and many people with type 2 diabetes eventually need insulin because of the duration of the disease and pancreatic fatigue.

Given the rapid increase in the number of people with this condition, and the increasingly younger age when the disease is diagnosed, healthcare providers need to be skilled in detection, management, education, and prevention strategies in order to decrease the overall burden on health and finances to patients and their families.

Gestational Diabetes

Gestational diabetes mellitus (GDM) is diabetes that develops for the first time during pregnancy and is seen as persistent hyperglycemia. Due to the overall stress of the pregnancy, and with additional risk factors similar to those of type 2 diabetes, such as obesity, sedentary lifestyle, high-fat diet, age, ethnicity, and genetic predispositions, almost 21% of all pregnancies may develop hyperglycemia.

Recommendations for GDM include:

- Screen for undiagnosed T2DM at the first prenatal visit in those with risk factors, using standard criteria.
- In pregnant women not previously known to have diabetes, screen for GDM at 24 to 28 weeks' gestation with a 75-g, 2h OGTT using the following stricter diagnostic cutoff points:
  - Fasting >92mg/dL in the morning after an overnight fast of at least 8 hours
  - 1 hour >180mg/dL
  - 2hour >153mg/dL
- If undiagnosed T2DM is suspected to have existed at the time of pregnancy, rescreen at 6 to 12 weeks' postpartum, using standard criteria.
- Women diagnosed with GDM should have lifelong screening for the development of T2DM or prediabetes at least every 3 years (ADA, 2012)

Other Types of Diabetes

Types of diabetes that fall into the "other" class of diabetes mellitus include MODY, LADA, endocrinopathies, and impaired fasting glucose (IFG).

MODY is a genetic mutation in an autosomal dominant gene that affects insulin production. Individuals with this diagnosis are generally children less than age 25 with a family history of diabetes for generations. These children still produce some insulin and are clinically closer to a type 2. They may or may not require insulin.

LADA presents in young adults in their twenties and can be confused as type 2 because of age; however, they do not produce any insulin and are clinically similar to type 1, requiring insulin. They have often been labeled as "diabetes 1.5" because they are clinically between type 1 and type 2.

Endocrinopathies may include polycystic ovarian syndrome, pancreatic cancer or tumors, and other hormonal disruptions in insulin production. Impaired fasting glucose presents as an FBG higher than 100 mg/dl but less than 126 mg/dl, so it does not qualify as full diabetes mellitus.

Types of Diabetes Mellitus					
	Type 1	Type 2	LADA	MODY	Other/IFG
Typical age of onset	Youth	Adult	Adult	Youth	Any age
Progression to insulin dependence	rapid	slow	Months/yrs	slow	varies
Presence of autoantibodies	Yes	No	Yes	No	No
Insulin dependence	Yes	No	Yes within years	Not always	varies
Insulin resistance	No	Yes	No	Yes	varies

Test Your Knowledge

A 34-year-old female patient presents with a symptoms of polyuria for 1 month and weight loss. Which diagnostic test is appropriate to diagnose this patient?

A. A fasting blood sugar (FBS) on one occasion
B. An A1C
C. A 2-hour postprandial
D. A random blood glucose (BG) with symptoms

Rationale: The FBS must be administered on two separate occasions, not just one. The A1C cannot be used because symptoms have only been reported for 1 month and the A1C is most accurate over 3 months. The 2-hour postprandial also requires two occasions. The random BG with symptoms is most helpful. Symptoms alone are not adequate because the polyuria may be caused by a urinary tract infection (UTI) or other problem.

Apply Your Knowledge

Explain in your own words, as if you were teaching a newly diagnosed patient with diabetes, what the difference is between the four classes of diabetes.

Answer: D

Regulation of Blood Glucose

Regulation of glucose in the body is done autonomically and constantly throughout each minute of the day. Normal BG levels should be between 60 and 140 mg/dL in order to supply cells of the body with its required energy. Brain cells don’t require insulin to drive glucose into neurons; however, there must still be normal amounts available. Too little glucose, called **hypoglycemia**, starves cells, and too much glucose (**hyperglycemia**) creates a sticky, paralyzing effect on cells. Euglycemia, or blood sugar within the normal range, is naturally ideal for the body’s functions. A delicate balance between hormones of the pancreas, intestines, brain, and even adrenals is required to maintain normal BG levels.

Fuels of the Body

To appreciate the pathology of diabetes, it is important to understand how the body normally uses food for energy. Glucose, fats, and proteins are the foods that fuel the body. Knowing how the pancreatic, digestive, and intestinal hormones are involved in food metabolism can help you understand normal physiology and how problems develop with diabetes.

Throughout the body, cells use glucose as a source of immediate energy. To keep the body running smoothly, a continuous concentration of 60 to 100 mg/dL of glucose in blood plasma is needed. During exercise or stress the body needs a higher concentration because muscles require glucose for energy (Basu et al., 2009). Of the three fuels for the body, glucose is preferred because it produces both energy and water through the Krebs cycle and aerobic metabolism. The body can also use protein and fat; however, their breakdown creates ketoacids, making the body acidic, which is not its optimal state. Excess of ketoacids can produce metabolic acidosis.

Functioning body tissues continuously absorb glucose from the bloodstream. For people who do not have diabetes, a meal of carbohydrates replenishes the circulating blood glucose about 10 minutes after eating and continues until about 2 hours after eating. A first-phase release of insulin occurs about 5 minutes after a meal and a second phase begins at about 20 minutes. Because the duration of insulin's effect is only about 2 hours, taking a 2-hour **postprandial** (after meal) BG shows how well insulin was released and used by the body. The food is broken down into small components including glucose and is then absorbed through the intestines into the bloodstream. Glucose (potential energy) that is not immediately used is stored by the body as glycogen in the muscles, liver, and fat.

Your body is designed to survive and so it stores energy efficiently, as fat. Most Americans have excess fat because they replenish the glucose stores by eating before any fat needs to be broken down.

When blood glucose levels fall after 2 hours, the liver replenishes the circulating blood glucose by releasing glycogen (stored glucose). **Glycogen** is a polysaccharide, made and stored primarily in the cells of the liver. Glycogen provides an energy reserve that can be quickly mobilized to meet a sudden need for glucose.

Hormones of the Pancreas

Regulation of blood glucose is largely done through the endocrine hormones of the pancreas, a beautiful balance of hormones achieved through a negative feedback loop. The main hormones of the pancreas that affect blood glucose include insulin, glucagon, somatostatin, and amylin.

Insulin (formed in pancreatic beta cells) lowers BG levels, whereas glucagon (from pancreatic alpha cells) elevates BG levels.

Somatostatin is formed in the delta cells of the pancreas and acts as the "pancreatic policeman," balancing insulin and glucagon. It helps the pancreas alternate in turning on or turning off each opposing hormone.

Amylin is a hormone, made in a 1:100 ratio with insulin, that helps increase **satiety**, or satisfaction and state of fullness from a meal, to prevent overeating. It also helps slow the stomach contents from emptying too quickly, to avoid a quick spike in BG levels.

As a meal containing carbohydrates is eaten and digested, BG levels rise, and the pancreas turns on insulin production and turns off glucagon production. Glucose from the bloodstream enters liver cells, stimulating the action of several enzymes that convert the glucose to chains of glycogen—so long as both insulin and glucose remain plentiful. In this postprandial or "fed" state, the liver takes in more glucose from the blood than it releases. After a meal has been digested and BG levels begin to fall, insulin secretion drops and glycogen synthesis stops. When it is needed for energy, the liver breaks down glycogen and converts it to glucose for easy transport through the bloodstream to the cells of the body (Wikipedia, 2012a).

In a healthy liver, up to 10% of its total volume is used for glycogen stores. Skeletal muscle cells store about 1% of glycogen. The liver converts glycogen back to glucose when it is needed for energy and regulates the amount of glucose circulating between meals. Your liver is amazing in that it knows how much to store and keep, or break down and release, to maintain ideal plasma glucose levels. Imitation of this process is the goal of insulin therapy when glucose levels are managed externally. Basal–bolus dosing is used as clinicians attempt to replicate this normal cycle.

While a healthy body requires a minimum concentration of circulating glucose (60–100 mg/dl), high chronic concentrations cause health problems and are toxic:

- **Acutely**: Hyperglycemia of >300 mg/dl causes polyuria, resulting in dehydration. Profound hyperglycemia (>500 mg/dl) leads to confusion, cerebral edema, coma, and, eventually, death (Ferrante, 2007).
- **Chronically**: Hyperglycemia that averages more than 120 to 130 mg/dl gradually damages tissues throughout the body and makes a person more susceptible to infections. The glucose becomes syrupy in the bloodstream, intoxicating cells and competing with life-giving oxygen.

The concentration of glucose in the blood is determined by the balance between the rate of glucose entering and the rate of glucose leaving the circulation. These signals are delivered throughout the body by two pancreatic hormones, insulin and glucagon (Maitra, 2009). Optimal health requires that:

- When blood glucose concentrations are low, the liver is signaled to add glucose to the circulation.
- When blood glucose concentrations are high, the liver and the skeletal muscles are signaled to remove glucose from the circulation.

Test Your Knowledge

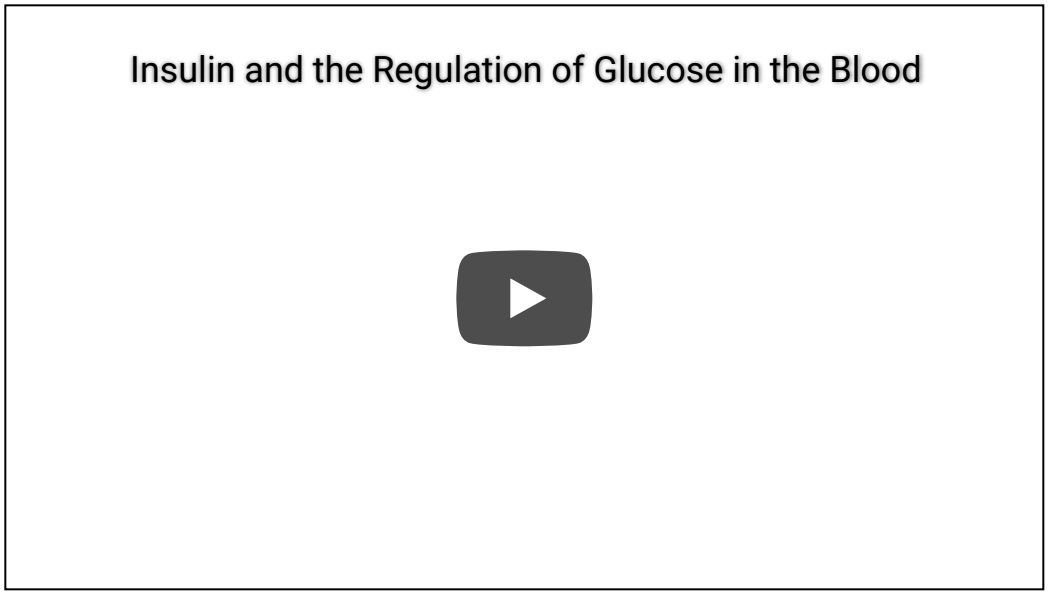
Glycogen is:

A. A hormone produced in the pancreas.
B. A polysaccharide that is stored in the liver.
C. Produced in the striated muscles when exercising.
D. An energy reserve that is slow to mobilize in an emergency.

Apply Your Knowledge

If you want to lose weight, what fuel would you decrease in your diet and what fuels would you increase?

Video (2:36)



https://www.youtube.com/watch?v=OlHez8gwMgw

Answer: B

The Role of Insulin

Insulin is a peptide hormone made in the beta cells of the pancreas that is central to regulating carbohydrate metabolism in the body (Wikipedia, 2016). After a meal, insulin is secreted into the bloodstream. When it reaches insulin-sensitive cells—liver cells, fat cells, and striated muscle—insulin stimulates them to take up and metabolize glucose. Insulin synthesis and release from beta cells is stimulated by rising concentrations of blood glucose. Insulin has a range of effects that can be categorized as **anabolic**, or growth-promoting.

Functions of Insulin	
Turns on	Turns off
Uptake and use of glucose by insulin-sensitive cells	Breakdown of glycogen in liver cells
Storage of glucose in the form of glycogen in the liver and skeletal muscle tissue. Storage of fat.	Breakdown of fat
Uptake of amino acids and the synthesis of proteins	Breakdown of protein
DNA synthesis	Gluconeogenesis

Test Your Knowledge

Insulin:

A. Is only available by injection or orally to treat T2DM.
B. Is a hormone that acts on the liver to convert excess glucose into glycogen.
C. Inhibits the uptake and use of glucose by skeletal muscles.
D. Is manufactured and secreted by the alpha cells of the pancreas.

Apply Your Knowledge

How would you explain the function of insulin to your patient with diabetes? What does it turn on and what does it turn off?

Answer: B

The Role of Glucagon

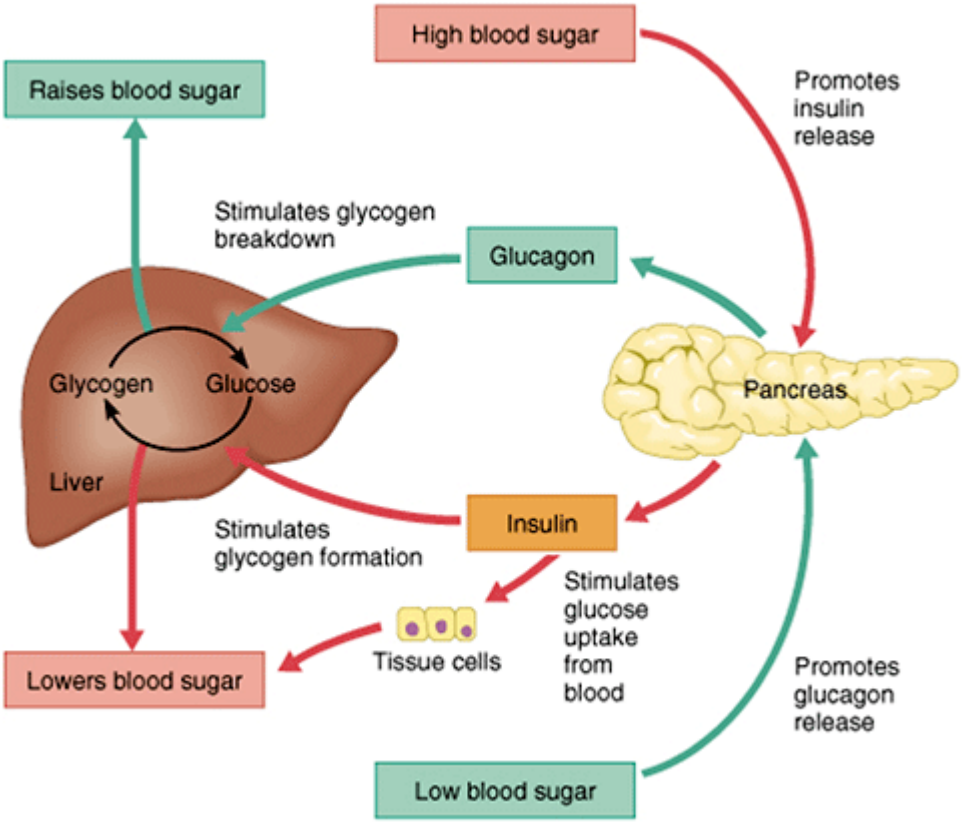
Glucagon, a peptide hormone secreted by the pancreas, raises blood glucose levels. Its effect is opposite to insulin, which lowers blood glucose levels. When it reaches the liver, glucagon stimulates **glycolysis**, the breakdown of glycogen, and the export of glucose into the circulation. In these ways, the effects of glucagon are **catabolic**, breaking down cells—the opposite of insulin's anabolic effects (Drucker, 2008).

The pancreas releases glucagon when glucose levels fall too low. Glucagon causes the liver to convert stored glycogen into glucose, which is released into the bloodstream. High BG levels stimulate the release of insulin. Insulin allows glucose to be taken up and used by insulin-dependent tissues, such as muscle cells. Glucagon and insulin work together automatically as a negative feedback system to keeps BG levels stable.

Glucagon is a powerful regulator of BG levels, and glucagon injections can be used to correct severe hypoglycemia. Glucose taken orally or parenterally can elevate plasma glucose levels within minutes, but exogenous glucagon injections are not glucose; a glucagon injection takes approximately 10 to 20 minutes to be absorbed by muscle cells into the bloodstream and circulated to the liver, there to trigger the breakdown of stored glycogen.

People with type 2 diabetes have excess glucagon secretion, which is a contributor to the chronic hyperglycemia of type 2 diabetes. The amazing balance of these two opposing hormones of glucagon and insulin is maintained by another pancreatic hormone called *somatostatin*, created in the delta cells. It truly is the great pancreatic policeman as it works to keep them balanced.

Complementary Roles of Insulin and Glucagon



After you've eaten, the concentration of glucose in your blood rises. When it goes too high the pancreas releases insulin into the bloodstream. This insulin stimulates the liver to convert the blood glucose into glycogen for storage. If the blood sugar goes too low, the pancreas release glucagon, which causes the liver to turn stored glycogen back into glucose and release it into the blood. Source: Google Images.

Test Your Knowledge

Glucagon:

A. Is a peptide hormone that is stored in the pancreas.
B. Is used to treat hyperglycemia by increasing the uptake of glucose in muscles.
C. Is a hormone that acts on the liver to convert glycogen back into glucose.
D. Stimulates the production of insulin.

Apply Your Knowledge

How is glucagon available by injection?

Answer: C

The Role of Amylin

Amylin is a peptide hormone that is secreted with insulin from the beta cells of the pancreas in a 1:100 ratio. Amylin inhibits glucagon secretion and therefore helps lower BG levels. It also delays gastric emptying after a meal to decrease a sudden spike in plasma BG levels; further, it increases brain **satiety** (satisfaction) to help someone feel full after a meal. This is a powerful hormone in what has been called the brain–meal connection.

People with type 1 diabetes have neither insulin nor amylin production. People with type 2 diabetes seem to make adequate amounts of amylin but often have problems with the intestinal incretin hormones that also regulate BG and satiety, causing them to feel hungry constantly. Amylin analogues have been created and are available through various pharmaceutical companies as a solution for disorders of this hormone.

The Role of Incretins

Incretins are glucagon-like peptides (hormones) made in cells of the small intestine and secreted into the circulation in response to food intake (Cernea & Raz, 2011). Incretins go to work even before blood glucose levels rise following a meal. They also slow the rate of absorption of nutrients into the bloodstream by reducing gastric emptying, and they may also help decrease food intake by increasing satiety.

People with type 2 diabetes have lower than normal levels of incretins, which may partly explain why many people with diabetes state they constantly feel hungry. After research showed that BG levels are influenced by intestinal hormones in addition to insulin and glucagon, incretin mimetics became a new class of medications to help balance BG levels in people who have diabetes.

Two types of incretin hormones are **GLP-1** (glucagon-like peptide) and **GIP** (gastric inhibitory polypeptide). Each peptide is broken down by naturally occurring enzymes called DDP-4, (dipeptidyl peptidase-4).

Exenatide (Byetta), an injectable anti-diabetes drug, is categorized as a glucagon-like peptide (GLP-1) and directly mimics the glucose-lowering effects of natural incretins upon oral ingestion of carbohydrates. The administration of exenatide helps to reduce BG levels by mimicking the incretins. Both long- and short-acting forms of GLP-1 agents are currently being used.

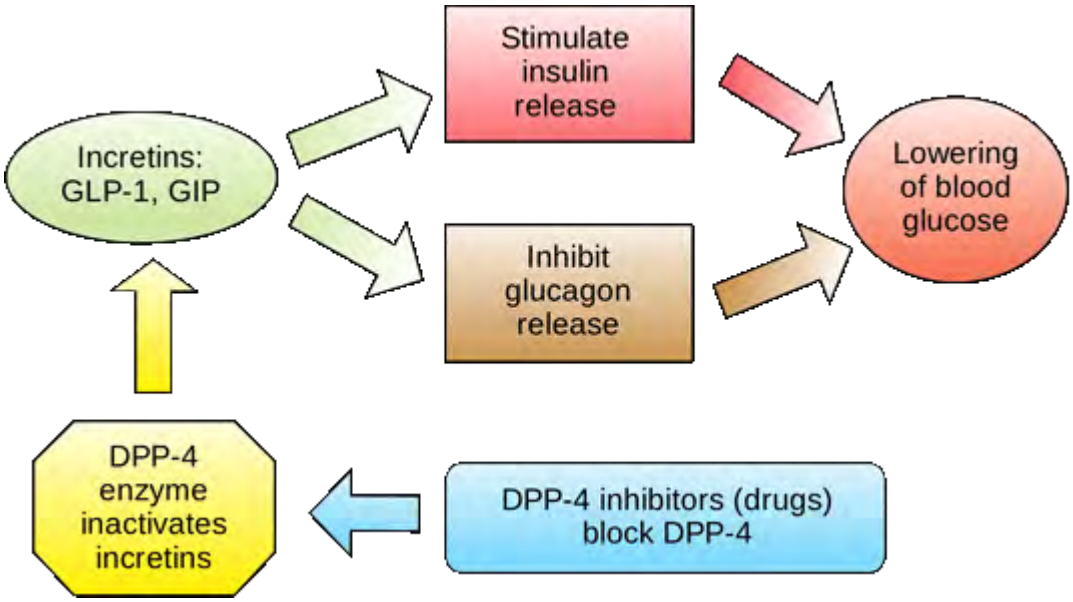
The functions of incretins are as follows:

- Stimulate insulin secretion
- Suppress glucagon secretion
- Slow gastric emptying to prevent spike in BG levels

- Increase satiety after a meal to signal to the brain to stop eating

Incretins are deactivated quickly by enzymes called DPP-4, in the bloodstream and on the surface of endothelial cells; thus, the glucose-lowering effects of incretins last only a few minutes (Drucker & Nauck, 2006). A new class of medications, called DPP4 inhibitors, block this enzyme from breaking down incretins, thereby prolonging the positive incretin effects of glucose suppression. An additional class of medications called dipeptidyl peptidase-4 (DPP-4 inhibitors—note hyphen), are available in the form of several orally administered products. These agents will be discussed more fully later.

Incretins Stimulate Insulin Release



Source: Wikimedia Commons.

Poor Regulation of Blood Glucose

People with diabetes have frequent and persistent hyperglycemia, which is the hallmark sign of diabetes. For people with type 1 diabetes, who make no insulin, glucose remains in the blood plasma without the needed BG-lowering effect of insulin. Another contributor to this chronic hyperglycemia is the liver. When a person with diabetes is fasting, the liver secretes too much glucose, and it continues to secrete glucose even after the blood level reaches a normal range (Basu et al., 2009).

Another contributor to chronic hyperglycemia in diabetes is skeletal muscle. After a meal, the muscles in a person with diabetes take up too little glucose, leaving blood glucose levels elevated for extended periods (Basu et al., 2009).

The metabolic malfunctioning of the liver and skeletal muscles in type 2 diabetes results from a combination of insulin resistance, beta cell dysfunction, excess glucagon, and decreased incretins. These problems develop progressively.

Early in the disease the existing insulin resistance can be counteracted by excess insulin secretion from the beta cells of the pancreas, which try to address the hyperglycemia. The hyperglycemia caused by insulin resistance is met by hyperinsulinemia. Eventually, however, the beta cells begin to fail. Hyperglycemia can no longer be matched by excess insulin secretion, and the person develops clinical diabetes (Maitra, 2009).

Test Your Knowledge

People with type 2 diabetes have:

A. Insulin sensitivity, which is an over-reaction of cells to insulin.
B. No beta cells in their pancreas and no circulating insulin at all.
C. Chronic hypoglycemia.
D. Insulin resistance, which is a decreased response of cells to insulin.

Apply Your Knowledge

How would you explain to your patient what lifestyle behaviors create insulin resistance?

Answer: D

The Problem of Insulin Resistance

In type 2 diabetes, many patients have body cells with a decreased response to insulin known as **insulin resistance.** This means that, for the same amount of circulating insulin, the skeletal muscles, liver, and adipose tissue take up and metabolize less glucose than normal. Being less sensitive to insulin, the liver does not react to the usual signal of insulin, so the liver manufactures and secretes more glucose than is needed (Huether & McCance, 2012).

Insulin resistance can develop in a person over many years before the appearance of type 2 diabetes. People inherit a propensity for developing insulin resistance, and other health problems can worsen the condition. For example, when skeletal muscle cells are bathed in excess free fatty acids, the cells preferentially use the fat for metabolism while taking up and using less glucose than normal, even when there is plenty of insulin available. In this way, high levels of blood lipids decrease the effectiveness of insulin; thus, high cholesterol and body fat, overweight and obesity increase insulin resistance.

Physical inactivity has a similar effect. Sedentary overweight and obese people accumulate triglycerides in their muscle cells. This causes the cells to use fat rather than glucose to produce muscular energy. Physical inactivity and obesity increase insulin resistance (Monnier et al., 2009).

The Problem of Beta Cell Dysfunction

For people with type 1 diabetes, no insulin is produced due to beta cells destruction. Research shows this is an autoimmune response gone awry, attacking the body's own cells. Triggers of that autoimmune response have been linked to milk, vaccines, environmental triggers, viruses, and bacteria.

For people with type 2 diabetes, a progressive decrease in the concentration of insulin in the blood develops. The continuously decreasing availability of insulin in type 2 diabetes is the direct result of a progressive worsening of the beta cells' ability to produce enough insulin when it is needed (Huether & McCance, 2012).

Not only do the beta cells release less insulin as type 2 diabetes progresses, they also release it slowly and in a different pattern than that of healthy people (Monnier et al., 2009). Without sufficient insulin, the glucose-absorbing tissues—mainly skeletal muscle, liver, and adipose tissue—do not efficiently clear excess glucose from the bloodstream, and the person suffers the damaging effects of toxic chronic hyperglycemia.

At first, the beta cells manage to manufacture and release sufficient insulin to compensate for the higher demands caused by insulin resistance. Eventually, however, the defective beta cells decrease their insulin production and can no longer meet the increased demand. At this point, the person has persistent hyperglycemia. In type 2 diabetes, beta cells seemingly exhaust their capacity to adapt to the long-term demands of peripheral insulin resistance (Huether & McCance, 2012).

A downward spiral follows. The hyperglycemia and hyperinsulinemia caused by the over-stressed beta cells create their own failure. In type 2 diabetes, the continual loss of functioning beta cells shows up as a progressive hyperglycemia.

Test Your Knowledge

In type 2 diabetes:

A. Beta cells in the pancreas cannot compensate for insulin resistance.
B. The pancreas is attacked by the body's immune system, resulting in pancreatitis.
C. The liver becomes overly sensitive to insulin.
D. Glucose cannot be used as fuel by any cells in the body.

Apply Your Knowledge

How would you explain insulin resistance differently to someone with type 1 diabetes and someone with type 2 diabetes?

Video (11:46)

https://www.youtube.com/watch?v=iTjDi2ZO0n8

Answer: A

Cell Damage in DM

Together, insulin resistance and decreased insulin secretion lead to hyperglycemia, which causes most of the health problems in diabetes. The acute health problems—diabetic ketoacidosis and hyperosmolar hyperglycemic state—are metabolic disorders that are directly caused by an overload of glucose. In comparison, the chronic health problems—eye, heart, kidney, nerve, and wound problems—are tissue injury, a slow and progressive cellular damage caused by feeding tissues too much glucose (ADA, 2015).

Hyperglycemic damage to tissues is the result of glucose toxicity. There are at least three distinct routes by which excess glucose injures tissues:

- Over time, excess glucose attaches to proteins in a process called **glycosylation**. For example, glycosylated hemoglobin (HbA1c), is the laboratory measure to monitor average glycemic levels. Glycosylated proteins trigger inflammatory reactions, which injure the lining of blood vessels. In addition, glycosylated proteins stick together on the basement membranes of capillaries, thickening the endothelial layers and disrupting their normal function.
- Excess intracellular glucose activates an enzyme called **protein kinase C**, which encourages the growth of unnecessary blood vessels, leads to blood vessel constriction, thickens basement membranes, and releases pro-inflammatory molecules such as C-reactive protein and homocysteine.
- Excess intracellular glucose reduces the effectiveness of the intracellular activities that protect against oxidants and oxidative stress. This leads to oxidative damage, especially in neurons. (Maitra, 2009)

Risk Factors for Diabetes Mellitus

As in any disease, there are modifiable and non-modifiable risk factors that cause the disease. Genetics, gender, ethnicity, and age are all noncontrollable. People with type 1 diabetes who have a genetic predisposition to a heightened and destructive autoimmune response cannot control it. People who are over 65 and of African American descent are at greater risk for developing type 2 diabetes, but cannot control those factors. Following a brief discussion of genetics we want to focus on the controllable risk factors that we can modify to prevent diabetes.

Genetic Factors

Genetics is like being handed a loaded pistol, but the lifestyle behaviors of obesity, overeating, sedentary lifestyle, and so on are what pull the trigger. It has been said 90% of all chronic diseases can be triggered or prevented by lifestyle choices, especially diet and exercise. A person’s genome is a strong determinant of the chance of developing type 2 diabetes. For example, if a dizygotic (fraternal) twin develops type 2 diabetes, the chances are about 25% that the other twin will also develop the disease. The disease risk doubles if the twins are monozygotic (identical): if a monozygotic twin develops type 2 diabetes, the chances are about 50% that the other twin will also develop the disease (Maitra, 2009). People with these genetic predispositions, however, do not always develop clinical diabetes.

It appears that, to develop type 2 diabetes, other health problems must intervene to activate or worsen the insulin resistance and beta cell dysfunction (Maitra, 2009). People with a genetic predisposition may be able to prevent the full development of the disease by health-promoting lifestyle behaviors that prevent overweight and obesity.

Type 2 diabetes is **polygenic**, meaning that it usually involves the expression of more than one problematic gene. More than twenty variant genes have been documented as potential contributors to the development of type 2 diabetes, and the problematic genes are found on a number of chromosomes. There is no single combination of genes that leads to type 2 diabetes. Instead, the expressions of a variety of combinations of problematic genes may create full development of type 2 diabetes.

"Accumulating data suggest that type 2 diabetes is likely a collection of many closely related diseases with varying but often overlapping primary mechanisms that involve both impaired insulin secretion and insulin resistance" (Grant et al., 2009).

Test Your Knowledge

Type 2 diabetes:

A. Is an inevitable disease of aging.
B. Is inevitable in people whose families have the disease.
C. May develop in genetically predisposed people with additional risk factors.
D. Is usually caused by the mutation of a single gene called T2D.

Apply Your Knowledge

Your patient wants to know why he developed type 2 diabetes. What risk factors would you review?

Answer: C

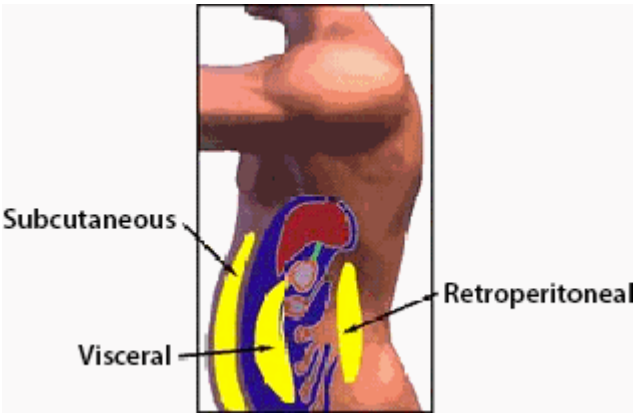
Controllable Risk Factors

Certain health problems are closely associated with the development of type 2 diabetes. These health problems are neither absolute nor independent causes of the disease; that is, not all people with these problems develop type 2 diabetes. Nonetheless, they are major risk factors because they help to initiate or to worsen type 2 diabetes in people with the predisposition for it.

Major risk factors for type 2 diabetes include obesity, physical inactivity, unhealthy diet, hyperglycemia, stress, and chronic inflammation.

Obesity

Excess body fat causes insulin resistance, and the risk for developing type 2 diabetes increases as the proportion of body fat increases. Body mass index (BMI) is used to measure the proportion of body fat to total body weight. The risk is higher when excess fat has accumulated inside the abdominal cavity, as opposed to under the skin. Excess intra-abdominal fat is a feature of more than 4 out of 5 patients with type 2 diabetes.



Fat that is inside the abdomen—visceral or intra-abdominal fat—differs metabolically from subcutaneous fat. Intra-abdominal fat is a risk factor for type 2 diabetes. A person's waist circumference is a good indicator of the amount of fat inside the person's abdomen (NHLBI, 2015).

Adipose tissue encourages insulin resistance in a number of ways. Excess fat, especially visceral fat, leads to higher blood levels of fatty acids, and fatty acids reduce glucose uptake, causing insulin resistance in skeletal muscle. Additionally, in obese individuals, adipose tissue releases less **adiponectin**, a hormone that reduces insulin resistance. Excess adipose tissue also secretes additional pro-inflammatory molecules (**cytokines**), which increase insulin resistance. The increased insulin resistance from all these causes leads to hyperinsulinemia, which further weakens dysfunctional beta cells (ADA, 2015).

Test Your Knowledge

A health problem that directly increases the risk of developing type 2 diabetes is:

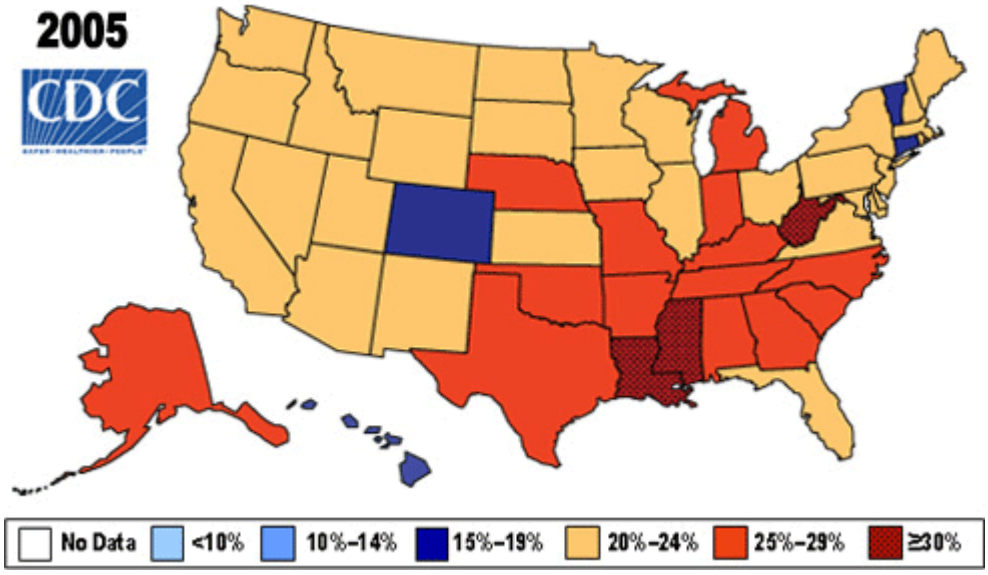
A. Intra-abdominal fat.
B. Periodontal disease.
C. Foot injuries.
D. Osteoporosis.

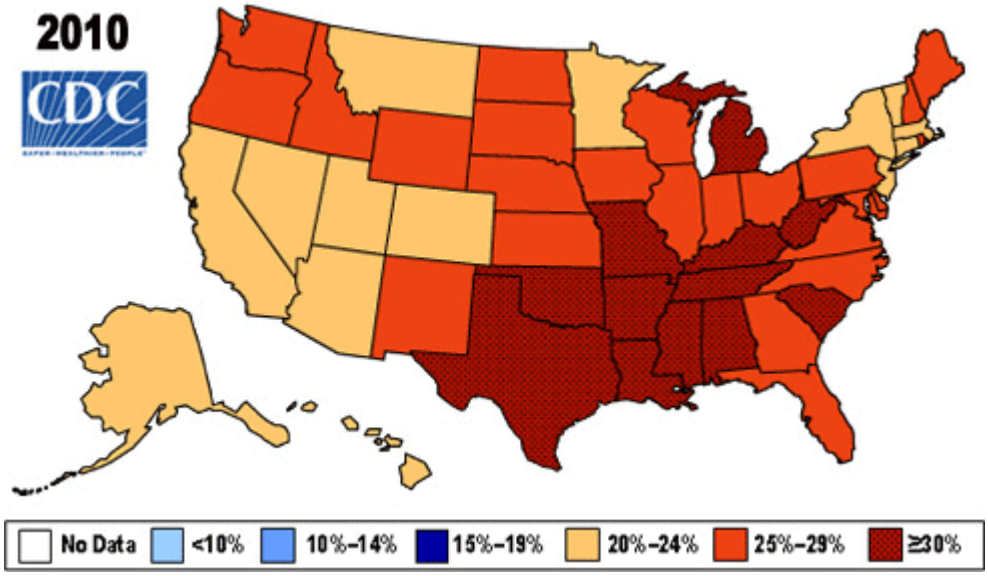
Apply Your Knowledge

What is the first behavior modification you should focus on for most people with type 2 diabetes?

Answer: A

Change in Prevalence of Obesity (by BMI) 2005–2010





Source: CDC.

Physical Inactivity

Physical inactivity is another major risk factor for the development of type 2 diabetes. In part, this results from the tendency of sedentary people to accumulate triglycerides in their muscle cells and gain weight.

Physical exercise is a powerful counterforce to insulin resistance. Regular exercise improves glycemic control and reduces the risk of developing cardiovascular complications in people with type 2 diabetes. “Furthermore, regular exercise may prevent type 2 diabetes in high-risk individuals” (ADA, 2015).

Poor Diet

Any dietary habits that lead to obesity also increase a person's chances of progressing from prediabetes to diabetes.

- A high-carbohydrate diet challenges the glucose-lowering ability of a person with prediabetes and accelerates the development of type 2 diabetes.
- A high-fat, low-fiber diet, especially one that includes saturated and trans fats, causes dyslipidemias, which worsen insulin resistance and foster the development of type 2 diabetes.

Hyperglycemia

A controllable risk factor of diabetes mellitus is progressive hyperglycemic states that can be caused by frequent high-carbohydrate consumption. Skeletal muscle and adipose tissue that become overloaded with glucose are less able to take up more glucose, thus hyperglycemia contributes to insulin resistance, prediabetes, and eventually diabetes (Buse et al., 2008).

Stress

Stress activates the sympathetic autonomic nervous system in the "fight or flight" reaction. **Cortisol**, known as the stress hormone from the adrenals, increases and acts as a counter-regulatory hormone to insulin. Cortisol elevates BG levels in an attempt to deliver glucose to muscle cells so as to fight the stressor. Chronic stress leads to chronic hyperglycemia, which in turn increases insulin resistance and triggers type 2 diabetes in predisposed people.

Chronic Inflammation

Type 2 diabetes alters the functioning of the immune system. Together, insulin resistance, hyperglycemia, and hyperinsulinemia create a persistent inflammatory reaction. At the same time, a chronic inflammatory state leads to chronic hyperglycemia, which then contributes to the progression of type 2 diabetes (O'Connor et al., 2006).

People who are in a constant state of emotional and physical stress are continually in a mild state of inflammation. Their blood shows persistent elevations of molecules of inflammation, such as C-reactive protein and interleukin-6. The pro-inflammatory cytokines causer an elevation in the level of adrenocorticotropic hormone (ACTH), which is the direct stimulant of cortisol secretion. Inflammation increases the level of blood glucose, causing hyperglycemia and eventual insulin resistance. Foods, injury, stress, and other disease processes can all create chronic inflammation.

Diagnosing Diabetes Mellitus

Signs and Symptoms of T2DM

Diabetes is diagnosed by documenting hyperglycemia through blood tests. In addition to blood tests, the initial examination of a patient suspected of having diabetes includes a history and physical examination that looks for signs of disease.

Clinical Presentation

Three symptoms—polyuria, polydipsia, and weight loss—have defined diabetes for centuries. This description written one hundred years ago still applies:

> The symptoms are usually gradual in their onset, and the patient may suffer for a length of time before he thinks it necessary to apply for medical aid. The first symptoms that attract attention are failure of strength, and emaciation, along with great thirst and an increased amount and frequent passage of urine. From the normal quantity of from 2 to 3 pints in the 24 hours it may be increased to 10, 20, or 30 pints, or even more. It is usually of pale colour, and of thicker consistence than normal urine, possesses a decidedly sweet taste, and is of high specific gravity. (Encyclopaedia Britannica, 1911)

In addition to the classic triad of polyuria, polydipsia, and weight loss, people with diabetes are often weak, frequently hungry between meals, may have blurred vision, and are prone to infections.

Hyperglycemia can present with vomiting, abdominal pain, dehydration, mental status changes, or coma (ADA, 2015). Many times people are newly diagnosed after presenting to an emergency department with acute symptoms that can mimic a flu.

Test Your Knowledge

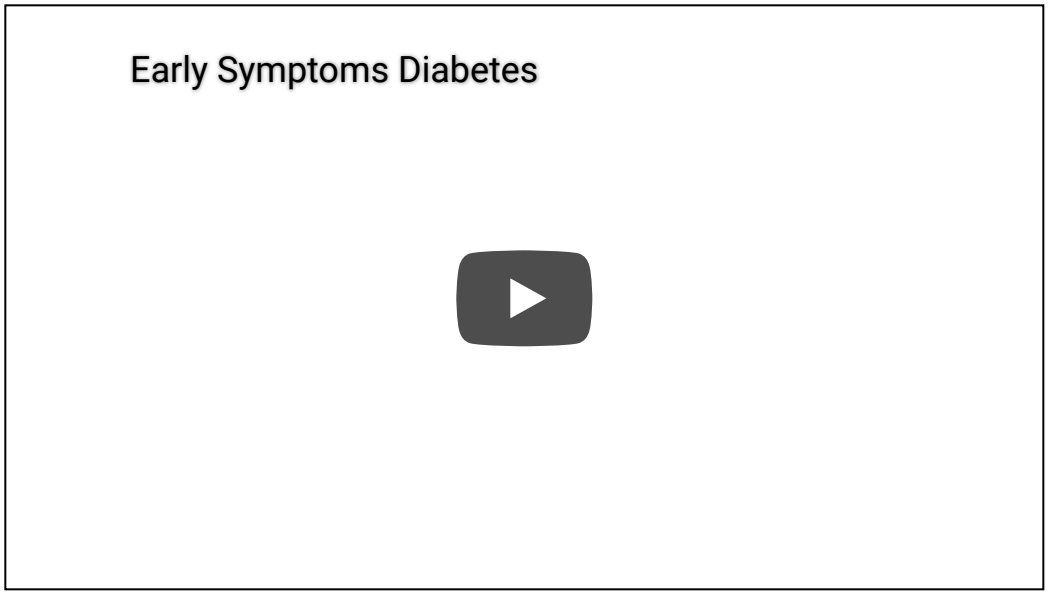
The classic triad of symptoms of diabetes is:

A. Gluconeogenesis, glycosuria, and glycolysis.
B. Blurry vision, dehydration, and mental status changes.
C. Macular edema, albuminuria, and seizures.
D. Polyuria, polydipsia, and weight loss.

Apply Your knowledge

What causes the three classic symptoms of diabetes?

Online Resource



https://www.youtube.com/watch?v=8BsYxprGn20

Answer: D

Medical History

The initial baseline workup of a patient with diabetes requires a review of illnesses, medications, family health history, lifestyle, and risk factors. The medical history should include:

Illnesses

Patient's current symptoms and when they began

- Results of any previous blood or urine glucose tests
- History of any episodes of diabetic ketoacidosis or hypoglycemia

- History of any diabetic complications:
  - Macrovascular (heart, arteries, stroke)
  - Microvascular (eyes, kidneys, nerves)
  - Infections or poor wound healing
  - Periodontal disease

Medications

History of all medicines currently taking

Family

Any family history of diabetes

Lifestyle

Level (to prepare for appropriate educational materials)

Physical Assessment

The initial physical examination focuses on signs of any health problems as well as developing diabetic complications. The exam includes:

- Height, weight, and calculation of body mass index (BMI)
- Blood pressure, including the blood pressure response to standing (orthostatic measurement) when autonomic dysfunction is suspected
- Funduscopic eye exam
- Skin exam for poorly healing injuries and signs of reduced circulation
- Foot exam, including palpation of pulses and tests of fine sensation (proprioception, vibration, light touch) and reflexes using a monofilament and tuning fork (ADA, 2015)

Laboratory Test Results

Blood Glucose Tests

The patient's blood glucose levels are used to diagnose and to monitor diabetes. Four glucose tests give a snapshot of a patient's current ability to regulate blood glucose levels:

- **Fasting plasma glucose (FPG)** is taken at least 8 hours after the patient has had any nourishment. Diabetes is characterized by an FPG >126 mg/dl.
- **Postprandial glucose level (PPG)** is taken 1 to 2 hours after a meal. Diabetes is characterized by any random PPG >200 mg/dl with symptoms.

- **Oral glucose-tolerance test (OGTT)** is a standardized postprandial glucose test. The OGTT is taken 2 hours after the patient has ingested 75g of oral glucose. Diabetes is characterized by an OGTT >200 mg/dl at the 2 hour time mark.
- **Glycosylated hemoglobin (A1c)** measures the saturation of hemoglobin molecules over the life of a red blood cell, which is 3 months. The normal range is 4-6 mg/dL.

A1c Values and Degree of Glycemic Control	
A1c value	Degree of blycemic control
<6.5%	Near normal
6.5–7.2%	Well controlled
7.3–9.3%	Moderately controlled
>9.3%	Poorly controlled

Source: Monnier et al., 2009.

In 2010 the American Diabetic Association adopted standards recommending the use of the A1c test to diagnose diabetes with a threshold set at 6.5%. The A1c test reflects the average glucose saturation over three months time and is strongly predictive of diabetic complications at higher levels.

The A1c has several advantages over the FPG and OGTT, including greater convenience because fasting is not required. A1c testing is recommended at the following intervals:

- Twice a year to measure overall control of diabetes
- Quarterly in the patient whose therapy has changed, or who is not meeting goals
- As needed, using Point of Care testing to make timely decisions regarding change of therapy

Anemia and hemoglobinopathies, such as sickle cell disease, may distort true results of A1c testing if the red blood cells are impaired. For conditions with abnormal red blood cell turnover such as pregnancy, recent blood loss, and transfusion, the diagnosis of diabetes must use one of the other three tests instead of A1c. If symptoms have not been present for three months prior to diagnosis, an A1c may not be accurate as it represents the average of three months.

Other Blood Tests

To assess for diabetic complications, baseline values are needed for:

- Fasting lipids (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides)
- Liver function tests
- Kidney function test (serum creatinine and glomerular filtration rate, GFR) (ADA, 2015)

Urine Tests

- Urinalysis for albumin (ADA, 2015)
- Urine for microalbumin (thought to be a more sensitive assay for albumin; an early indicator of diabetic nephropathy)

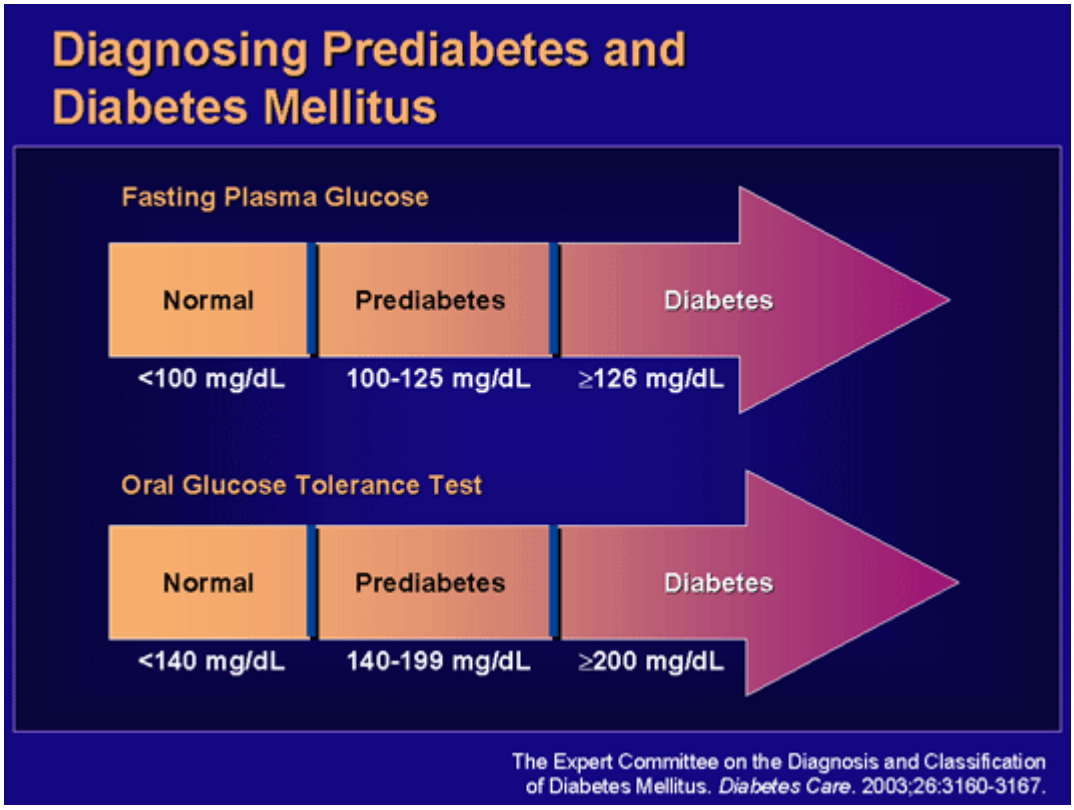
Prediabetes and Metabolic Syndrome

Diagnosing Prediabetes

By identifying patients with prediabetes, it is possible to intervene to prevent diabetes and its complications and improve future health. Prediabetes is diagnosed by the same blood sugar screening lab tests as diabetes. The person's blood sugar levels will show a higher BG than the normal range but below full diabetes, which is between 100 and 125 mg/dL. It is estimated 86 million Americans over age 20 have prediabetes, which is 1 out of every 3 adults (FDA, 2015).

Prediabetes may not manifest with acute symptoms and is mainly detected by blood glucose screening tests. Any of four criteria can be used to diagnose prediabetes: impaired fasting glucose BG > 100–125 mg/dL, impaired glucose tolerance >140–199 mg/dL, A1c >5.7%, <6.5% and positive screening of three abnormalities that qualify as metabolic syndrome:

- **Impaired fasting glucose**, which is a fasting plasma glucose level between normal and diabetes
- **Impaired glucose tolerance**, which is an oral glucose-tolerance test result between normal and diabetes
- **Presence of three of the five disorders of metabolic syndrome**



The chance that a person with prediabetes will progress to type 2 diabetes is high. A person without prediabetes has about a 5% chance of developing diabetes in six years. In contrast, a person with an FPG and an OGTT in the prediabetes range has about a 65% of developing diabetes in six years (Garber et al., 2008).

Managing Prediabetes

The goals of treating prediabetes are to slow its progression into type 2 diabetes and to reduce the person's chance of developing cardiovascular disease or microvascular complications (retinopathy, nephropathy, and neuropathy) (Garber et al., 2008).

Step one in treating prediabetes is intensive lifestyle management. Without lifestyle changes, 15% to 30% of people with prediabetes will progress to type 2 diabetes within five years (CDC, 2015). The same principles and education are used to treat diabetes.

The first recommendation is **weight loss**: a weight loss goal of 5% to 10% to be achieved by reducing the person's intake of calories and increasing the person's physical activity. Weight loss medications have often been given to help reach this goal; however, the FDA strongly cautions patients about many such pharmaceuticals. Because lifestyle modification and healthy living behaviors can be difficult to maintain for many people, most of them progress to needing pharmacologic assistance for weight loss and lowering BG.

The following cautions are included on weight-loss drugs for prediabetes and T2DM:

- **Sibutramine (Meridia).** In October 2010 the FDA recommended against further use of this drug, as it is associated with unnecessary cardiovascular risks to patients. The manufacturer (Abbott) voluntarily agreed to stop marketing in the United States.
- **Orlistat (Alli, Xenical).** In May 2010 the FDA approved a revised label for this drug to include rare but severe liver injury in some people. Some cases have resulted in liver transplant or death. Research shows it reduced the incidence of diabetes by almost 40% in obese people (Torgerson et al., 2004).
- **Qsymia** (extended-release combination of naltrexone and bupropion). Among other side effects, the manufacturer reports increased incidence of metabolic acidosis and hypoglycemia in diabetic patients who take medication to control hyperglycemia, making it a less than ideal agent for this population.
- **Belviq (lorcaserin**). The drug has potential for addiction, and may cause heart valve and mental problems and low blood sugar.

Step two in treating prediabetes is **anti-diabetic drug therapy**, especially for patients at high risk for developing diabetes complications. High-risk patients include those with metabolic syndrome, current cardiovascular disease, progressively worsening hyperglycemia, nonalcoholic fatty liver disease, a history of gestational diabetes, or polycystic ovary syndrome. **Metformin** has been approved for the treatment of prediabetes by the FDA and is a top tier medication after lifestyle behavior modification, which should include exercise and meal planning education. **Acarbose** has also been shown to reduce the risk of coronary heart disease and promote weight loss. Other pharmaceutical agents, including amylin analogues and incretin mimetics, have joined the arsenal for physicians to use for people with prediabetes.

People with prediabetes are given the same health coaching and guidance as those with diabetes, and management is focused on behavioral change for healthy lifestyles. Patients with prediabetes should also be treated to reach the same lipid and blood pressure goals as patients with diabetes.

Test Your Knowledge

Prediabetes:

A. Is diagnosed when the fasting blood glucose level is >126 mg/dl.
B. Usually precedes type 2 diabetes.
C. Presents with the same triad of symptoms as diabetes.
D. Is not a threat to patients and need not be treated.

Apply Your Knowledge

What national and state health programs are available to help decrease the rising incidence of prediabetes?

Answer: B

Diagnosis of Metabolic Syndrome

Metabolic syndrome is a group of risk factors that raise your risk of heart disease, diabetes, and stroke. The term *metabolic* refers to the biochemical processes of a body that is functioning normally. **Metabolic syndrome** identifies a person as having dysfunctional metabolic processes that put the person at risk for comorbidities. The American Heart Association (AHA) and National Heart, Lung, and Blood Institute (NHLBI) identify metabolic syndrome if there are any three of these five criteria:

Waist circumference

Large waistline (>40 inches in men; >30 inches in women)

For people of non-Asian origin

>102 cm in men or >88 cm in women

For people of Asian origin

>90 cm in men or >80 cm in women

High triglycerides

>150 mg/dl or on medicines for high triglycerides

Low HDL cholesterol

<40 mg/dl for men, <50 mg/dl for women, or on medicines for low HDL cholesterol

High fasting blood glucose

>100 mg/dl or diagnosed with diabetes or prediabetes

Blood pressure	>130 mm Hg systolic or >85 diastolic or on medicines for hypertension

Managing Metabolic Syndrome

Heart disease is the most common cause of death for people with metabolic syndrome and type 2 diabetes, and the reduction of cardiovascular risk is a top priority. A number of interrelated disorders significantly increase anyone's chance of developing cardiovascular diseases, with the resulting possibility of myocardial infarction or stroke. These disorders include:

- Central (intra-abdominal or visceral) obesity
- Insulin resistance, type 2 diabetes, or hyperglycemia
- Dyslipidemias (high blood levels of triglycerides, high blood levels of small dense LDL cholesterol particles, and low blood levels of HDL cholesterol)
- Hypertension

While a person can have any one of these problems, each of these cardiometabolic disorders promotes and worsens the others. For example, insulin resistance can lead to hyperlipidemia and hypertension; hypertension increases the likelihood of developing diabetes; and central obesity can lead to insulin resistance and diabetes. People tend to have more than one of these disorders at a time (Buse et al., 2008). Treatment of the metabolic syndrome involves the separate treatment of each of its components, such as diet, exercise, and weight loss, which collectively impact each other.

Test Your Knowledge

Metabolic syndrome is:

A. An autoimmune disease.
B. No longer accepted as a medical term.
C. A cluster of components that must be treated individually.
D. A single disorder that puts a person at risk for psoriasis.

Apply Your Knowledge

How can you teach your patients about the lifestyle changes to decrease metabolic syndrome?

Answer: C

The Diabetes Healthcare Team

People with diabetes mellitus can often feel alone and overwhelmed by all that is needed to manage diabetes. The reality is that millions of people are available to help provide education and resources and they should be considered part of their own healthcare team.

The traditional approach to patient care was to see the patient as sick and helpless, forced to be compliant with the prescribed medical regimen. A new era has refreshingly changed the paradigm to **patient-centered**, with all efforts to help increase self-management using the resources and tools provided by the team. The ADA has, in fact, declared the focus of diabetes education to be self-management, not mere compliance with a physician.

Team members include the primary care provider, nurses, diabetes educators, dieticians, podiatrists, optometrists, pharmacists, social workers, and more. The diabetes patient is the day-to-day disease manager on the team. For example, a licensed nurse with special training and education can teach each patient how to check daily BG levels, how to take medications, and how to care for injuries and wounds. A dietician can help the patient learn how to plan a healthy and manageable nutrition plan based on their culture, food preferences, and economic limitations.

In addition, a patient with diabetes should see an ophthalmologist or optometrist for an annual dilated eye exam. The patient should have regular dental exams. Kidney, artery, or foot problems should be monitored by the appropriate specialists. If the patient is having psychological or mood problems, a mental health professional should be involved (ADA 2015). The patient should be referred to a certified diabetes educator, who is a health professional devoted to helping the patient achieve self-care behaviors and positive behavioral change toward health. Each of these professionals is a part of the whole patient team.

Diabetes self management education (DSME) is focused on behavior change. A critical part of caring for people with diabetes is teaching them the overall treatment plan and how to care for themselves (ADA, 2015). People with diabetes have better outcomes when they understand their disease and have the skills and coaching to manage their lives so as to keep their BG levels as close to normal as possible (Strine, 2005). Those people who have not received formal diabetes self-management education have knowledge gaps, don’t receive preventive services, and are more prone to develop chronic complications (Kent, 2013; Strine, 2005).

Certified diabetes educators (CDEs) have additional education and training regarding diabetes mellitus and are generally covered under insurance benefits. A certified diabetes educator (CDE) is a nurse, pharmacist, physician, social worker, or dietician who must take a certifying exam after 1,000 qualifying hours of working in diabetes education. Advanced practice nurses, physicians, those with prescribing abilities, and those who have a master's degree in diabetes education may choose to take the board certification exam to earn the BC-CDE designation, which focuses on management of diabetes. Public health workers, health coaches, and non-certified diabetes educators, such as dieticians and nurses without the certification, can be a tremendous support in promoting behavior change.

The ADA and the American Association of Diabetes Educators (AADE) have developed similar DSME programs that includes focus on seven topics and self-care behaviors:

1. Healthy eating
2. Physical activity
3. Medication management
4. Monitoring
5. Problem solving
6. Reducing risks of acute and chronic complications
7. Psychosocial aspects of living with diabetes.

The AADE has coined them the AADE7 self-care behaviors. An ADA-approved diabetes self-management educational program focuses on empowering the person with diabetes to achieve the following:

- Understand the basics of diabetes and its treatment
- How to plan nutritious meals
- How to incorporate physical exercise into daily life
- The importance of smoking cessation
- How to take diabetes medicines properly and safely
- How to prevent, recognize, and cope with acute complications of diabetes
- How to prevent, recognize, and cope with chronic complications of diabetes
- How to prevent, recognize, and cope with social and psychological difficulties caused by diabetes
- Stress management

Click here for an online resource of the National Certification Board for Diabetes Educators.

Treatment Strategies for Diabetes

This is the best time in the history of the world to have diabetes because there are so many treatment strategies, pharmacologic options, and resources. The overall goal for a person with diabetes is to learn to live as full and healthy a life as possible within their physical limitations and to avoid complications. Research concludes that keeping blood glucose levels as close to normal as possible will help them achieve this goal. Strategies to reach the overall goal focus on glycemic control through improved healthy living behaviors.

Medical care of diabetes begins with a baseline medical evaluation. The patient's current degree of glucose control is assessed, the presence and state of any diabetes complications are documented, and any aggravating conditions, such as obesity or physical inactivity, are evaluated. Diabetes is a life-long illness, and people need a life-long plan for diabetes self-management. It is crucial that the patient be a part of the goal making and not subject to some isolated notations by a physician.

As with any complex health issue, a diabetes care plan begins with a problem list that can be managed by a physician or diabetes educator. Each item on the list is assigned a goal, and a specific strategy for reaching the goal. For diabetes, the problem list begins with "controlling blood glucose levels," the goal might be "lower A1c to <6.5%," and the strategy would include "weight loss, increased exercise, dietary changes, and (possibly) medications."

Next, each existing diabetic complication is listed. One item on the list, for example, might be "glaucoma," the goal might be "reduce daily ocular pressure to <22 mm Hg," and the strategy might be "refer to an ophthalmologist." Potential complications are also listed; for example, one might be "at risk for kidney damage," and the goal might be "watch for indications of kidney dysfunction," and the strategy might be "schedule annual serum creatinine level measurements, calculate corresponding GFRs, and test urine for albumin."

Another example of a medical goal is "elevated triglycerides (250 mg/dl)," and the goal would be "lower triglycerides to <150 mg/dl," and the strategy might be "weight reduction, low-fat diet, and increased physical activity."

The full problem list with its goals and strategies needs to be shared with the patient and, ideally, the care team. The provider and the patient will both have the overall plan in mind and will be able to monitor its progress and share its successes. The patient must be involved with the goal making process or success will be limited.

The Primary Goal: Glycemic Control

The degree to which a patient's blood sugar level is closely regulated is called the patient's **glycemic control**. Poor glycemic control leads to chronic hyperglycemia, which is the underlying cause of diabetic health problems. The first priority of diabetes care is to strengthen glycemic control.

FPG and PPG Levels

Reducing hyperglycemia is the goal of diabetic disease control. The degree of a patient's hyperglycemia—the level of glycemic control—is monitored in two ways:

- The average degree of glycemic control can be followed by measuring the patient's blood concentration of glycosylated hemoglobin, HbA1c. This test represents a more stable average blood glucose over the preceding 120-day period.
- The current degree of glycemic control can be followed by measuring the daily levels of blood glucose before breakfast and after a meal. Home glucose monitors, which require ever-smaller amounts of blood to produce a reliable readout, have improved this aspect of management; however, these values fluctuate to a considerable degree during the course of a day.

One way to monitor a patient's glycemic control is to chart and monitor **fasting plasma glucose (FPG)** and **postprandial blood glucose (PPG)** levels. These measurements are taken by the patient, and the patient or a family member should learn to use a home glucose meter. The American Diabetes Association (ADA, 2015) recommends that most adult patients should aim to maintain goals of:

- FPG (fasting plasma glucose) = 70–130 mg/dl and
- Peak PPG (postprandial glucose) = <180 mg/dl

All patients with diabetes should learn to monitor their own blood glucose with a glucose meter and be given time to practice in front of a diabetes educator to confirm the correct procedure. Regular monitoring can provide feedback to patients of how activity, emotions, and meals affect their BG levels. Research provides evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c (Miller et al., 2013). People can make needed daily adjustments by knowing their glucose number throughout the day rather than just in the doctor's office every 3 to 6 months.

Patients taking diabetes medications, especially insulin, should also be taught how to adjust their medications, diet, and activity in response to hypoglycemia and hyperglycemia.

Technology has greatly strengthened the ability to measure BG throughout the day due to the **continuous glucose monitor (CGM).** Normally the body regulates BG through constant feedback between insulin, glucose, somatostatin, and chemoreceptors in the blood that measure blood osmolarity (concentration of particles). People with diabetes have lost effective autoregulation, which results in chronic hyperglycemic episodes. CGM consists of a glucose sensor, a transmitter, and a small external monitor that allow us to view BG levels in real time. A small needle is inserted in subcutaneous tissue and shows glucose trends in tissue fluid. CGM is available through several manufacturers but is more expensive than conventional home BG meters. CGM provides helpful information to patients managing their own BG levels, especially those with hypoglycemic unawareness who may not recognize symptoms when their BG is dropping.

There are dozens of blood glucose monitors that have different features and costs. Each January the ADA publishes in their *Diabetes Forecast* magazine a full consumer guide of meters currently on the market, which can be helpful in comparing devices and products.

A1c Levels

Another good measure of glycemic control is the patient's A1c level. The American Diabetes Association (ADA, 2015) recommends that adult non-pregnant patients should aim to maintain a goal of A1c <6.5%. Lowering A1c to below or around 6.5% has been shown to reduce microvascular and macrovascular complications of type 1 and type 2 diabetes.

A1c values show the average glucose level for the past three months, so swings between hyperglycemia and hypoglycemia, are smoothed out, which may not be the true picture. It is important that people taking insulin have more immediate feedback about their blood glucose concentration, so daily FPG and PPG monitoring is crucial. Current research also concludes that overall BG control after meals appears to be a more powerful indicator of overall glycemic control than FPG levels.

Test Your Knowledge

An A1c is the:

A. Typical fasting glucose level during the past few months.
B. Blood glucose level 2 hours after ingesting 75 g of glucose.
C. Average level of blood glucose over the past three months.
D. Blood glucose level after >8 hours of no caloric intake.

Apply Your Knowledge

How would you explain to your patient that they should be testing BG throughout the day to receive better feedback about their body's response to food, activity, emotions, and medications?

Answer: C

Blood Glucose Meters Reference

http://www.diabetesforecast.org/2015/mar-apr/images/glucose-meters-2015-revised8-7.pdf

7 Strategies for Improving Glycemic Control

Diabetes is a progressive disease. In the prediabetic stage, a patient's metabolic compensatory mechanisms may be able to avoid significant periods of hyperglycemia. When people with T2DM no longer have the ability to keep their blood glucose levels within a near to normal range, adequate glycemic control can usually be maintained with a healthy diet, weight reduction, and increased physical exercise.

Treatment for T2DM typically begins with therapeutic lifestyle changes:

- An education program for patient self-management
- A weight reduction plan
- An individualized plan for medical nutrition
- An individualized exercise regimen
- A schedule of regular follow-up and monitoring visits

Based on the ADA and AADE's 7 Self-Care Behaviors, the seven strategies for improving glycemic control are listed in the box below.

7 Self-Care Behaviors

1. Weight loss
2. Meal planning
3. Movement or exercise
4. Monitoring
5. Medications
6. Stress management
7. Prevention of complications

Weight Loss

Weight loss is often of primary importance. Excess weight is a direct cause of insulin resistance, and, as the excess weight increases, the glycemic control decreases. When the excess fat is visceral (inside the abdomen as opposed to directly under the skin), the diabetogenic effect is worse (Maitra, 2009). Eighty to ninety percent of people with type 2 diabetes are overweight, and a weight loss of 5% to 10% of the person's body weight will decrease:

- Average blood glucose levels
- Excess glucose secreted by the liver
- Excess blood insulin that appears during fasting
- Overall insulin resistance

One of the first steps in helping an overweight person regain better control of their BG levels is to encourage them to lose weight. Formal weight loss programs that include low-calorie diets, behavior modification, and regular exercise have been shown to produce sufficient weight loss to improve the glycemic control of overweight patients with T2DM. An effective goal is a 5% to 10% weight loss (Joffe & Yanagisawa, 2007).

There are no magic weight loss diets, and it is always necessary to reduce people's daily calories for them to lose weight. In the long run, low-carbohydrate diets (<130 g carbohydrates) seem to be about as effective and as safe as low-fat diets, but without intensive effort either variety of diet typically produces only modest weight loss (ADA, 2015). For those with type 2 diabetes who are very obese and have a BMI >35 kg/m2, bariatric surgery may be considered, because in many cases it can dramatically improve the patient's glycemic control (ADA, 2015).

Meal Planning

The patient's diet is an important component of the plan to keep blood glucose levels under control. An organized approach to a patient's overall diet and eating habits is called **medical nutrition therapy (MNT).** In medical nutrition therapy, registered dieticians specializing in diabetes work with patients to plan both meal content and eating schedules. The goals are to minimize hyperglycemic episodes and to fit the proper meals into the patient's lifestyle. Appropriately planned eating has been shown to reduce the A1c levels of patients with type 2 diabetes by 2% to 3% in 6 months.

Although numerous studies have attempted to identify the optimal mix of macronutrients for meal plans of people with diabetes, it is unlikely that one such combination of macronutrients exists. The best mix of carbohydrate, protein, and fat appears to vary depending on individual circumstances (ADA, 2015).

Diets must be tailored to individual patients. Nonetheless, there are some general principles that can be used as a starting point for patients with T2DM, such as knowing the basic macronutrients of carbohydrates, fats, and proteins and the micronutrients of vitamins and minerals (ADA, 2015). General recommendations include:

Calories

- Reduction in total calories is usually needed.

Fats

- Reduction in total fats is helpful.
- Most important is the reduction in saturated fatty acids, trans fatty acids, and cholesterol. Saturated fat should be <7% of total daily calories. Trans fats should be reduced as close to zero as possible.

Carbohydrates

- Carbohydrates should be limited to about 130 g/day, divided among all the meals.
- When eating a varied diet, patients need to estimate the carbohydrate content of many different meals. For this, carbohydrate counting or carbohydrate exchange rules are two methods that can be used and taught.

Fiber

- Dietary fiber is an important part of any diet plan.
- The current recommendations are 14 g of dietary fiber per day for every 1,000 calories of food; this is 25 g of dietary fiber daily for women and 38 g for men (Amer. Diet. Assoc., 2015)

Miscellaneous Foods

- Sugar alcohols and nonnutritive sweeteners can be used in moderation.
- Alcohol should be limited to 1 drink/day for women and 2 drinks/day for men.
- Antioxidant supplements (vitamin C, vitamin E, or carotene) are recommended only if evidence of deficiency is seen.
- Chromium supplements are recommended only if a deficiency is seen. (ADA, 2015)

Test Your Knowledge

A healthy diabetic diet should include:

A. Chromium supplements.
B. Antioxidant supplements.
C. At least 260 g of carbohydrates daily.
D. Less than 7% of daily calories as saturated fats.

Apply Your Knowledge

What is your current consumption of calories, fats, proteins, carbohydrates, fiber, water, vitamins, and minerals? How is your nutrition?

Answer: D

Exercise

Movement and exercise helps patients with type 2 diabetes control their blood glucose levels and reduces their risk of developing cardiovascular disease. The minimum recommendation is 30 minutes of moderate-intensity physical activity 3 days every week. Brisk walking is an example of moderate-intensity physical activity. The positive effects of exercise on glycemic control last for 2 to 3 days, but it is recommended that people exercise at least every other day.

Exercise can temporarily create hyperglycemia as muscles use up existing blood glucose and the liver releases stored glycogen to sustain the activity. Monitoring BG levels before exercise, and every hour for long-term activity, is important to avoid hypoglycemia. If BG levels are >200 mg/dL it is recommended to increase water consumption and carefully monitor BG throughout activity to avoid further elevating BG levels.

At the other extreme, hypoglycemia can be a problem. Some people with T2DM who are taking insulin or insulin secretagogues will become hypoglycemic with exercise. People with generally good glycemic control are least likely to develop severe hypoglycemia. Those patients who tend to get hypoglycemic easily can prepare for exercise by lowering their insulin dose or by increasing their carbohydrate intake before exercising.

Other conditions require diabetic patients to check with their doctor before beginning an exercise program. Patients with severe peripheral neuropathy can unknowingly damage their feet during exercise that is hard on their lower limbs. In addition, severe retinopathy is sometimes a reason to avoid vigorous bouncing or head-lowering type exercise.

Exercise programs should be tailored to each patient. For example, people who have been sedentary should begin their exercise program at low intensity and gradually increase the amount and time of their physical activities (Marwick et al., 2009).

To have a significant effect, regular activity must become a continuing part of a patient's life. Human nature reveals we stick to exercise goals more consistently when the activities are in a structured setting and when we report our progress to someone, such as attending regular classes and reporting the record. Health professionals and diabetes educators can encourage patients to just move more in their daily activities. Finding activities that fit into their daily habits, meet their preferences, and that they enjoy will bring the best rewards.

Test Your Knowledge

For type 2 diabetes, lifestyle interventions (weight reduction, increased exercise, improved diet) are:

A. First-line therapy.
B. Most effective for those less than 50 years old.
C. Most effective when used in combination with insulin supplements.
D. Used for their psychological effect, to give patients a role in their care.

Apply Your Knowledge

What are you doing for your own exercise plan? In what ways can you increase your movement in your daily life?

Answer: A

Monitoring

Monitoring is a strategy for overall diabetes management but it includes much more than just monitoring blood glucose levels. It also means to monitor blood pressure, lipid levels, A1c, weight, BMI, liver function, kidney function, skin and foot care, infections, vision, and overall health condition. It is highly recommended that a patient with diabetes follow up regularly with the primary care provider for evaluation of glycemic control, prevention of complications, and treatment for any additional comorbidities.

Medications

Medication management often becomes necessary for glycemic control even after lifestyle modification efforts have been made. Over time, T2DM worsens, and the degree and frequency of hyperglycemia increase into a range that threatens tissue damage, resulting in eye, kidney, nerve, and artery problems. When therapeutic lifestyle changes become insufficient to maintain good glycemic control for T2DM, it is time to consider medications. Physicians, APNs, and PAs have more options to consider when prescribing antihyperglycemic medications.

In the past the only options were injectable insulin and oral sulfonylureas. Today, over nine classes of medications are available, with multiple brands and dosages within each class of drugs. The goal of all medications used to manage diabetes is to maintain glucose levels as near normal as possible while minimizing the danger of hypoglycemia or other adverse effects.

Effectiveness of any antihyperglycemic medication is measured by a drop in A1c levels. The higher the baseline A1c, the greater the expected reduction (Triplitt, 2014).

Impact of Pharmaceuticals on A1c Levels		
< 1%	1%–1.5%	>1.5%
DPP-4 inhibitor Sulfonylurea TZD SGLT2 inhibitor	GLP-1 receptor agonist	Insulin

Commonly Prescribed Oral Medications to Reduce Hyperglycemia in T2DM

Oral anti-hyperglycemic drugs

Action: slows absorption of carbohydrates from the intestines

- Alpha-glucosidase inhibitors
- Acarbose (Prandase, Precose)
- Miglitol (Glyset)

Biguanides

Action: decreases liver glucose release and decreases insulin resistance

- Metformin (Fortamet, Glucophage, Glumetza, Riomet and combination drugs)

Dopamine agonist

Action: thought to affect circadian rhythm to decrease obesity and insulin resistance.

- Bromocriptine (Parlodel)

DPP-4 inhibitors

Action: prolongs action of incretins to slow BG absorption

- Alogliptin (Nesina)
- Alogliptin & pioglitazone (Oseni)
- Linagliptin (Tradjenta)
- Saxagliptin (Onglyza)
- Sitagliptin (Januvia)
- Sitagliptin and simvastatin

Glucagon-like peptides

Action: similar to natural incretin. Increases insulin secretion, slow stomach emptying and reduces appetite.

- Albiglutide (Tanzeum); weekly
- Dulaglutide (Trulicity); daily
- Exenatide (Byetta); twice daily
- Exenatide extended release (Bydureon); weekly

- Liraglutide (Victoza); daily

Meglitinides

Action: stimulate insulin release from the pancreas.

- Repaglinide (Prandin)
- Nateglinide (Starlix)

SGLT2 inhibitors

Action: promotes glucose excretion through urine

- dapagliflozin (Farxiga)
- canagliflozin (Invokana)
- empagliflozin (Jardiance)

Sulfonylureas (second-generation)

Action: increase insulin secretion from the pancreas

- glimepiride (Amaryl)
- glimepiride and pioglitazone (Duetact)
- glimeperide and rosiglitazone (Avandaryl)
- gliclazide
- glipizide (Glucotrol)
- glyburide (DiaBeta, Glynase, Micronase)
- chlorpropamide (Diabinese)
- Tolazamide (Tolinase)
- Tolbutamide (Orinase, Tol-Tab)

Thiazolidinediones (TZDs)

Action: decreases insulin resistance through improved muscle uptake of glucose

- Pioglitazone (Actos)
- Rosiglitazone (Avandia)

Oral Medications for Reducing Hyperglycemia

Learning the diabetes medications alphabetically or by the organ they act on can be a helpful strategy because the number of pharmaceutical agents has more than doubled in the past decade. Knowing the organ and site of action will also help you remember the side effects as alterations in the action site often produce adverse effects in that same location.

Alpha-glucosidase inhibitors act on the intestines to slow the absorption of food. Therefore, gas, bloating, and intestinal discomfort are common. It's also important to note that a patient taking an alpha-glucosidase inhibitor won't respond quickly to a fast-acting sugar to treat hypoglycemia because the medication will blunt its absorption. Instead of taking a fast-acting glucose, these patients should consume milk (a lactose sugar), which won't be blocked and can help treat hypoglycemia.

Biguanides are the first-tier medication suggested by the ADA and AACE after lifestyle modification. The generic *metformin* has similar or superior effects to second-generation sulfonylureas and to the more expensive TZDs and meglitinides. Metformin acts on several action sites including the liver and skeletal muscle cells, so liver function tests must be done annually and the patient should be taught the symptoms of lactic acidosis. Metformin tends to cause less weight gain than other diabetes medicines. It also poses a smaller risk of adverse events than second-generation sulfonylureas and TZDs. Therefore, noninsulin drug treatment of T2DM typically begins with metformin (AACE, 2015).

Combination therapies may be more effective than single-drug therapies and, when metformin is not sufficient to keep A1c levels under 6.5%, another medication may be added. Currently, no one drug is recommended as the best addition to metformin. Healthcare providers (HCPs) choose by balancing cost, drug side effects, and the individual patient's tolerance for the medicine. HCPs and patients can feel comfortable using older medications such as metformin and second-generation sulfonylureas, as monotherapy or in combination, before newer diabetes medications such as DPP4 inhibitors or meglitinides, especially when cost is a factor (Bolen et al., 2007).

The dopamine agonist known as *bromocriptine* has been added to the list of FDA-approved medications for diabetes and recognized by the ADA despite incomplete understanding of its action. It appears to act on regulating the body's circadian rhythms, which can help improve metabolism and control weight.

DPP-4 inhibitors act on the enzyme that degrades incretin hormones in the intestines. They enhance the action of the incretin hormones, which slows the absorption of sugars in the intestines. Interestingly, side effects include respiratory problems such as nasopharyngitis, nasal stuffiness, and headache. The DPP-4 agents are taken orally on a daily basis.

Glucagon-like peptides are called **incretin mimetics**, whereas DPP-4 inhibitors are known as **incretin enhancers**. Both of these agents offer important advantages over previously used drugs for T2DM. They both promote weight loss (or are weight neutral) by slowing gastric emptying and increasing satiety. Both inhibit glucagon secretion and counter regulatory mechanisms. Use of these agents as monotherapy has a low association with hypoglycemia and there is no recommendation for increased self-monitoring of blood glucose (SMBG); however, when used in combination with a secretagogue or insulin, more frequent monitoring of blood glucose is recommended (ADA, 2015). GLP-1s and DPP-4s preserve beta-cell function and secretion, which has the potential to slow the progression of the disease. The GLP-1 agents are injectables with varying dosing schedules that range from qd and bid to weekly (qw) dosing. Adverse affects include nausea, vomiting, diarrhea, gastric and intestinal distress and lipodystrophies from injections.

Clinical trials and post marketing reports have identified additional safety risks that are under active investigation for the incretin-based therapies. Pancreatitis has been reported with each of the agents, but a clear association has not yet been established; it should be noted that people with T2DM already have a three-fold higher incidence of pancreatitis compared to normoglycemic control.

GLP-1 agents are being studied for a potential association with medullary thyroid cancer. These agents should be avoided where a family history of this cancer exists.

Renal safety is an additional consideration with the GLP-1 agents and the DPP-4 agent saxagliptin. In general, saxagliptin has safety considerations with all the more serious adverse-effect categories: pancreatitis, cardiovascular effects, hypersensitivity, renal and hepatic events, and increased risk for bone fracture compared to other agents in this group.

Meglitinides act on the pancreas to promote insulin secretion in the pancreas just as the sulfonylureas do, which puts them at greater risk for causing hypoglycemia.

Sodium-glucose transporter 2 inhibitors (GLT2) are a new class of drugs that act in a completely new way to lower blood glucose. This class acts by blocking kidneys from excreting sucrose into the bloodstream. Within the last five years, the FDA has approved new drugs in this class for use in T2DM. Invokana is taken as an oral agent, once daily. Invokana was approved by the FDA based on nine studies involving more than 10,000 patients. The trial showed improvement in both A1c and fasting plasma glucose. Invokana may be used alone or in combination with other agents to control T2DM.

The most common side effects seen with this agent are yeast infections and urinary tract infections arising from increased amounts of sugar in the urine. An additional side effect was hypotension due to the increased excretion of fluids. The FDA noted that the drug may carry some increased heart risks during the first 30 days of use, suggesting the need for increased surveillance and careful patient selection. Invokana is only recommended for patients with T2DM and should not be used in those patients who have severe renal impairment or end-stage renal disease, or for those receiving dialysis.

For decades, sulfonylureas had been the only oral option for T2DM. Each new generation improved the potency and reduced adverse affects. The most critical adverse affect, however, is hypoglycemia, because this class increases insulin excretion from the pancreas. It is, naturally, not approved for T1DM because those patients have no insulin to be stimulated. Sulfonylureas come in combination with many of the other classes of medications and can be used as mono, dual, or triple therapy.

Thiazolidinediones (TZDs, as they are commonly known) are a class of medication introduced in the early 1990s to treat T2DM. TZDs act by increasing muscle cell sensitivity to endogenous insulin and adverse effects have been noted in muscular organs such as the heart muscle. As a group, these drugs have had an interesting history characterized by initial high hopes alternating with strong warnings or being removed from the market altogether.

The first agent in this class, troglitazone (Rezulin) was taken off the market in the late 1990s due to an increased incidence of drug-induced hepatitis. For several years following the removal of troglitazone, no TZDs were in common use.

In 1999 rosiglitazone (Avandia) was introduced to the market. As post marketing information began to accumulate that showed an increased association with coronary events—including heart attack, edema and congestive heart failure (CHF)—it came under closer scrutiny. In September 2010, rosiglitazone was withdrawn from the market in Germany and France and placed under restrictions in the United States due to these cardiovascular effects. In February 2011, the FDA issued an advisory that no new patients be started on this agent, and consideration be given regarding patient preference that they be switched to another drug in the class, pioglitazone (Actos). In the spring of 2011, pioglitazone had a warning issued due to an increased association with bladder cancer when used over 12 months. Germany and France pulled pioglitazone from the market in June 2011.

Currently there are restrictions and warnings on the two drugs in this class that are still available with regard to their ability to cause or worsen CHF, as well as the association of Actos with bladder cancer. Clinicians are advised to carefully consider the risks and benefits of TZDs as well as combination products containing them. The following is a summary of the combination products that include a TZD:

- Avandamet: Avandia + metformin (restricted access)
- Avandaryl: Avandia + Amaryl (restricted access)
- ActoplusMet: Actos + metformin
- Duetact: Actos + Amaryl

Test Your Knowledge

Of the oral anti-diabetic medications:

A. Insulin tablets are usually first to be added to a regimen of therapeutic lifestyle interventions.
B. Metformin is usually the first to be added to a regimen of therapeutic lifestyle interventions.
C. The second-generation sulfonylureas (glimepiride, glipizide, glyburide) are no longer prescribed.
D. Secretagogues are considered too risky to be used outside of a hospital setting.

Apply Your Knowledge

Identify the affected organ of each class of medications.

Answer: B

Non-Insulin Injectable Antihyperglycemics

Amylin analogue (mimetics)

Action: slows stomach emptying, suppresses appetite and improves weight loss, reduces liver glucose production.

- Pramlintide (Symlin); with meals

Glucagon-like peptides

Action: similar to natural incretin. Increases insulin secretion, slow stomach emptying and reduces appetite.

- Albiglutide (Tanzeum); weekly
- Dulaglutide (Trulicity); daily
- Exenatide (Byetta); twice daily
- Exenatide extended release (Bydureon); weekly
- Liraglutide (Victoza); daily

Amylin analogues are synthetic imitations of the naturally occurring amylin produced in the pancreas and administered by injection. Just as insulin cannot (yet) be given orally due to stomach acid, which makes oral ingestion ineffective, amylin must be given by injection. Pramlintide (Symlin) has many of the same incretin actions of the GLP-1 agents, except that it does not stimulate insulin secretion; it acts by slowing gastric emptying, thus suppressing glucagon release by the liver. It also promotes earlier satiety, with the result that fewer calories are consumed, leading to subsequent weight loss.

Similar to the other GLP-1 agonists, Symlin is administered as a subcutaneous injection prior to meals. Also similar to the GLP-1 agents, it is associated with significant nausea, which may limit the ability to administer the agent at therapeutic doses. Symlin may be used for patients with either T1DM or T2DM. When the patient is also receiving insulin, the dose may need to be lowered. Pramlintide (Symlin) carries a black box warning for severe hypoglycemia 3 hours post injection. For patients who are not sensitive to symptoms of hypoglycemia, known as *hypoglycemic unawareness*, this is not an ideal agent. Nevertheless, in a carefully selected population, the lowering of the HgA1c by up to 1% and the associated weight loss may result in significant improvement in overall management of diabetes.

Glucagon-like peptides, a kind of incretin hormone, act to slow glucose absorption in the intestines and buffer the spike of blood glucose after a meal. This class of medication must be taken by injection, and patient instruction includes teaching the difference between this and insulin, especially if they are also taking insulin. The most recent improvements in antidiabetic pharmaceuticals has been this class because the potency now allows once a week injection, which increases patient adherence. Adverse affects are found in the intestines, however, as this is the organ of action.

Use of Insulin in T2DM

As type 2 diabetes continues it follows a downward spiral and the pancreatic beta cells weaken considerably. At some point, the beta cells secrete so little insulin that adequate glycemic control requires the patient to take insulin (ADA, 2015). The following table summarizes types of insulin commonly used with T2DM.

Insulins: Onset, Peak, and Duration					
Type	Brand	Onset	Peak	Duration	Notes
Ultra Rapid-Acting					
Inhaled insulin	Afrezza	1–2 min	15–20 min	2–2 ½ hr	Inhaled. Must have spirometry done. Contraindicated for COPD/asthma.
Rapid-Acting					
Lispro Aspart Glulisine	Humalog Novolog Apidra	10–30 min	30–90 min	3–6 hr	Insulin for meals. Taken with the meal. Can be used in insulin pumps.
Short–Acting					
Regular insulin	Humulin R Novolin R	30 min–1 hr	2–5 hr	5–8 hr	Need to take 30–60 min before meals.
Regular insulin (concentrated)	Humulin R U-500	30 min		up to 24 hr	For pts who require >200 units/day
Long-Acting					
Glargine Detemir	Lantus Levemir	1–2 hr	No peak	20–24 hr	Long-acting, covers insulin needs for a full day. Not to be mixed with any other insulin.
Pre-mixed/combination					
Human insulin	Humulin 70/30	30 min	2–4 hr	14–24 hr	These products are combinations of short- and intermediate-acting insulin in one bottle or pen. They are
	Novolin 70/30	30 min	2½ hr		
	Humulin 50/50	30 min	2–5 hr		

Insulins: Onset, Peak, and Duration					usually taken 2–3 x daily before meals.
Type	Brand	Onset	Peak	Duration	Notes
Insulin lispro	Humalog 50/50	15–30 min	45–120 mins		
	Humalog 72/25	30 min			
Insulin aspart	Novolog 70/30	10–20 min	1–4 hrs		

Insulin Schedule Management

Clinicians vary in the way they start insulin in people who have type 2 diabetes. One common regimen begins by adding a long-lasting insulin injection once daily to the existing oral medication(s). The ideal regimen of insulin is the basal-bolus method because it provides the best physiologic action and control. However, many patients are reluctant to adopt a more complicated routine, so introducing insulin using a simpler strategy improves adherence.

Choice of insulin and timing of injection is influenced by many factors, including the patient's visual acuity and coordination to correctly draw the dose, the ability to titrate and calculate doses, and coordination with individual lifestyle factors. Additional factors include patient work environment, cost and coverage, cultural influences, and other medical comorbidities. All of these factors need to be evaluated and will influence the decision to use a basal insulin once daily, or to supplement this further with premix or meal coverage.

If the patient is to be started on insulin by adding a basal dose, it is given in the evening along with the regimen of oral agents. This strategy is associated with less nighttime hypoglycemia. Insulin detemir is associated with less weight gain than insulin glargine. For most patients with T2DM, the initial daily dose can be weight-based at 0.15 units/kg/day (0.1–0.2 units/kg/day is the recommended range). Ultimately, most patients will require significantly more due to the high levels of insulin resistance and overweight or obesity in this population. Basal insulin is titrated upward slowly to achieve a fasting level in the 100 mg/dl range. For example, a patient weighing 200 lbs requires approximately 44 units of glargine along with metformin and perhaps a second oral antihyperglycemic agent in order to achieve optimal glycemic control.

In a highly motivated population, the addition of a mealtime insulin (lispro, aspart, or glulisine) will allow for better glycemic control and add some flexibility, as doses are tied to mealtimes and match the pattern of post meal BG levels. The first prandial dose is matched to the largest meal and then titrated to other meals as the patient gains confidence in self-management. This process depends upon the patient's being sensitive to symptoms of hypoglycemia, along with a willingness to do more frequent self-monitoring blood glucose (SMBG) and injections. When using a prandial insulin, the patient must understand that the rapid-onset insulins must be covered with adequate carbohydrate intake in order to prevent hypoglycemia.

Another routine that may be appropriate is the use of premixed insulins, which combines a rapid-acting and intermediate analog (NovoLog, Humalog) in varying concentrations. Premixes are an appropriate intermediate-intensity strategy for patients who need improved glycemic control to achieve target HgA1c, but who desire a simpler routine that requires less frequent SMBG and insulin injections only twice daily. Patients who are selected for this method need to assess frequently for hypoglycemia. They should also keep a fairly consistent routine with regard to mealtimes. Initial dosing is tied to the largest meal of the day with a second dose added at breakfast once it is determined that the patient can safely and reliably follow the routine.

Ultimately, choice of insulin depends on many factors, including patient and provider preference, convenience, willingness, and the ability of the patient to consistently inject insulin one or more times per day. Continuing the patient on metformin assists in improving insulin sensitivity because it reduces gluconeogenesis. Continuing sulfonylureas (glimepiride, glipizide, glyburide) carries a greater risk for hypoglycemia and should be discontinued. GLP-1 analogs such as exenatide can be continued.

Avoid using insulin as a "threat" when patients have difficulty achieving target goals because this will further alienate them from both the provider and the process. Focus instead on the goal of continuing to have the most satisfying and healthy life possible.

Test Your Knowledge

Most patients with type 2 diabetes:

A. Should take insulin supplements as soon as they are diagnosed.
B. Will need insulin supplements after taking oral medications for more than a decade.
C. Should not take insulin supplements due to increased risk of infection at injection sites.
D. Have better glycemic control and no additional risk if insulin is taken along with metformin and a sulfonylurea.

Apply Your Knowledge

How would you explain the different kinds of insulins to a patient?

Answer: B

Other Major Goals: Managing Comorbidities

Dyslipidemia and hypertension are two health problems commonly found in patients with type 2 diabetes. These comorbidities need special attention because they markedly increase a patient's risk of developing cardiovascular disease, which is the major cause of death in people with diabetes.

Dyslipidemia

The most prevalent lipid abnormality in patients with T2DM is a decreased level of HDL cholesterol. Healthy target levels of HDL are >40 mg/dl in men and >50 mg/dl in women, and people with type 2 diabetes frequently have HDL blood levels below the target values. These patients also tend to have blood triglyceride levels above the healthy target level of <150 mg/dl. In addition, many patients with type 2 diabetes have blood levels of LDL cholesterol above the healthy target level of <100 mg/dl.

This group of dyslipidemias—low HDL cholesterol, high triglycerides, and high LDL cholesterol—gives a diabetes patient a high risk of developing cardiovascular disease, with resulting myocardial infarction, heart failure, or stroke. For the purpose of setting LDL target levels, diabetes is considered as great a risk factor as known cardiac disease in establishing the need for anti-lipid therapy. The ADA now encourages the use of statins in cholesterol lowering efforts (ADA, 2015).

The therapeutic lifestyle interventions used to improve glycemic control will also push lipids toward healthy target levels. When lifestyle changes do not achieve the blood lipid goals, medication should be added. For heart health, the primary goal is a reduction in LDL levels, and the recommended drug for lowering LDL cholesterol is a statin (eg, Lipitor).

Cardiovascular disease (CVD) is such a serious threat to people with T2DM that they should take statins even when their lipid levels meet the targets, under the following conditions:

- The patient already has cardiovascular disease, or
- The patient has other risk factors for cardiovascular disease, such as hypertension or abdominal obesity.

Blood Lipid Goals for People with Diabetes

- LDL cholesterol <100 mg/dl
- HDL cholesterol >40 mg/dl in men, >50 mg/dl in women
- Triglycerides <150 mg/dl

Source: ADA, 2015.

Test Your Knowledge

Cardiovascular disease (CVD) is such a serious threat to people with type 2 diabetes that a patient should generally be given a lipid-lowering drug (a statin) if the patient has:

A. Type 2 diabetes and another risk factor for CVD, such as hypertension or abdominal obesity.
B. Type 2 diabetes and a family history of type 2 diabetes.
C. Prediabetes.
D. Prediabetes and a family history of type 2 diabetes.

Apply Your Knowledge

What nutrition and exercise guidelines could you teach to a patient to help lower LDL and increase HDL?

Answer: A

Hypertension

Hypertension (high blood pressure) is a frequent companion to diabetes; approximately 75% of people with type 2 diabetes have hypertension. In part, this correlation is a direct complication of diabetes. Chronic hyperglycemia causes a thickening and stiffening of the walls of arterioles, and in turn causes hypertension (Maitra, 2009). As with dyslipidemia, hypertension puts a person with type 2 diabetes at higher risk for cardiovascular disease.

Blood Pressure Goals for People with Diabetes

- Systolic <130 mm Hg
- Diastolic <80 mm Hg

Therapeutic lifestyle changes are the first-line treatment. When lifestyle changes do not lower blood pressure sufficiently, medication should be used. In type 2 diabetes, drug therapy for hypertension begins with either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) such as valsartan. (ACE inhibitors and ARBs should not be given to pregnant women.)

Often, it will be necessary for patients with diabetes to take two or more medications to reduce their blood pressure below 130/80 mm Hg. If the patient's kidney function is not impaired, the second drug is usually a thiazide diuretic (ADA, 2015).

Test Your Knowledge

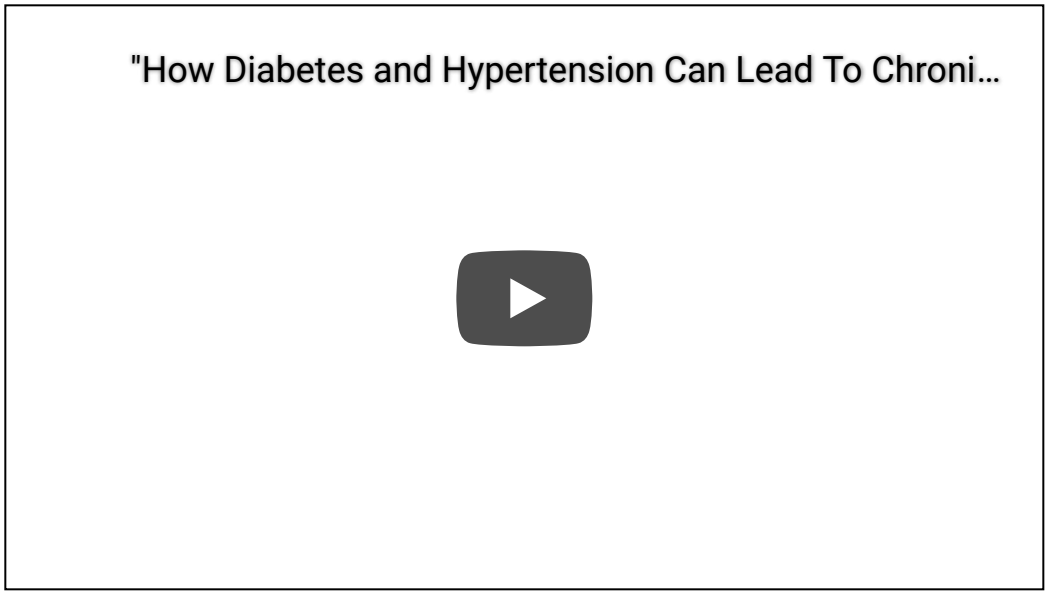
In patients with type 2 diabetes, high blood pressure is:

A. Uncommon, being found in <25% of those with diabetes.
B. Typically treated using insulin supplements.
C. The most common cause of death (as listed on death certificates).
D. Considered to be >130/80 mm Hg.

Apply Your Knowledge

What daily behaviors would you teach a patient about how to lower blood pressure?

Video (4:49)



How Diabetes and Hypertension Can Lead to Chronic Kidney Disease
https://www.youtube.com/watch?v=6fXe_ulHgCk

Answer: D

Prevention of Infectious Diseases

The American Diabetes Association (ADA, 2015) recommends that patients with type 2 diabetes get a yearly influenza vaccination and a one-time pneumococcal vaccination.

A pneumococcal revaccination is recommended for patients if their first vaccination matched two criteria:

1. The vaccination was given >5 years ago, and
2. The vaccination was given when the patient was <65 years old

Test Your Knowledge

People diagnosed with type 2 diabetes should get:

A. A rubella vaccination booster.
B. A tetanus vaccination booster.
C. Yearly influenza vaccinations.
D. Yearly pneumococcal polysaccharide vaccinations.

Apply Your Knowledge

What are the various kinds of flu shots and which one would you recommend to a patient with diabetes who has an egg allergy?

Answer: C

Psychosocial Problems

The continuous presence and progression of a chronic illness like diabetes creates real psychological stress. Chronic illnesses also strain finances, productivity, and relationships. Over time, even resilient patients can become fatigued, depressed, or anxious, especially when the disease worsens or when complications appear. In addition, individuals with schizophrenia and bipolar disorder are at increased risk for developing T2DM and are often more difficult to manage when diabetes is diagnosed (AACE, 2011). Individuals who are receiving antipsychotic agents such as respiradyne, quetiapine, olanzapine, and others for chronic symptoms should be monitored for weight gain and screening for T2DM because these medications can cause hyperglycemia.

At each visit, doctors and other members of the diabetes team should ask patients about their mood, their current view of their disease, and the effect of diabetes on their family and finances. The team should also be aware of signs of psychosocial problems. These signs include:

- The appearance of eating disorders
- Changes in the patient's mental abilities
- Mood changes
- Depression or anxiety
- The appearance of relationship problems
- Poor compliance with their therapy regimen
- Unexpected hospitalizations

The diabetes team is responsible for helping a patient emotionally as well as medically, and the appearance of psychosocial problems is a sign that the patient should be referred to a mental health professional (ADA, 2015). Support groups, online forums, and even Facebook groups have numerous resources to help and encourage people with diabetes. Advocacy groups such as The Juvenal Diabetes Research Foundation (JDRF) has annual walkathons and promotes diabetes awareness, and social media sites can help patients feel supported and not alone.

Test Your Knowledge

Especially when the disease worsens, type 2 diabetes can cause:

A. Schizophrenia.
B. Depression or anxiety.
C. Megalomania.
D. Neurosis.

Apply Your Knowledge

What support groups and online resources can you share with a person who has diabetes?

Online Resource

AADE Patient Resource Guide

Answer: B

Acute Illnesses

Stresses, such as illnesses, injuries, or surgery, trigger the release of the stress hormone *cortisol*, which causes hyperglycemia. People with type 2 diabetes who normally have well-regulated blood glucose levels may not have sufficient glycemic control to counteract the added hyperglycemia of stress and short-term illness.

During sick days, patients should check their blood glucose levels more frequently. People who take insulin may need more than their usual doses of insulin and those who are noninsulin-dependent type 2 can temporarily require supplemental insulin. People with diabetes who are ill should be especially careful not to get dehydrated as they are more likely to need hospitalization. Diabetes patients should be advised to consult their physician when they become sick or injured (ADA, 2012).

Hospitalizations

People who are hospitalized for any reason have more in-hospital difficulties if they develop hyperglycemia from any cause. For example, hyperglycemia is associated with worse outcomes from strokes, heart attacks, and surgery.

Even when they normally have good glycemic control, hospitalized patients with type 2 diabetes are at risk for developing hyperglycemia. First, the stresses of illness or surgery cause hyperglycemia. Second, when hospitalized, a patient's usual medications may have to be changed or withheld. Third, drugs such as glucocorticoids or vasopressors may be administered, which elevate blood glucose levels (Moghissi et al., 2009).

While in the hospital, patients with diabetes should have their blood glucose levels monitored regularly before meals to give meal coverage of insulin, and hospital personnel should be aware of the hypoglycemia protocol. Patients on continuous intravenous insulin typically require hourly blood glucose testing until the blood glucose levels are stable, then every 2 hours (ADA, 2015). Communicating the diagnosis of DM and the most recent BG between hospital staff in perioperative settings or change of shift is hugely valuable to avoid hypoglycemic episodes and complications.

Blood Glucose Targets for Hospitalized Diabetes Patients

For most patients

- Fasting blood glucose <126 mg/dl, with other pre-meal values <140 mg/dl
- Random blood glucose <180–200 mg/dl

For critically ill patients

For nonsurgical patients

- Random blood glucose <140 mg/dl

For surgical patients

- Random blood glucose should be kept close to 110 mg/dl

For critically ill patients, hyperglycemia should be controlled with a tested intravenous insulin protocol that is known to be safe.

Source: ADA, 2015; Moghissi et al., 2009.

Test Your Knowledge

When patients with type 2 diabetes are hospitalized for other reasons:

A. They tend to do well on their regular regimen of oral medications and only have problems when they become hypothermic.
B. Hyperglycemia is a secondary consideration, especially in critically ill patients, and high blood glucose levels can be tolerated for a few days when necessary.
C. They should always be put on IV insulin and their blood glucose levels should be monitored daily.
D. Their blood glucose levels should be monitored regularly and hyperglycemia should be corrected with insulin, not with oral medications.

Apply Your Knowledge

What is the hypoglycemic protocol for your facility?

Answer: D

Acute Complications of T2DM

In patients with type 2 diabetes, either extremely high or extremely low blood glucose can cause an acute diabetic emergency.

- Too much circulating glucose leads to a hyperosmolar hyperglycemic state (HHS) or diabetic ketoacidosis (DKA).
- Too little circulating glucose causes hypoglycemia.

Hyperglycemic Crises

Uncontrolled hyperglycemia can lead to a physiologic crisis of dehydration, electrolyte imbalance, and confusion or coma. Hyperglycemic crises are typically triggered by physical stress, such as an illness, injury, stroke, or myocardial infarction, which causes a sudden persistent hyperglycemia. Without the help of a knowledgeable caregiver, this sudden hyperglycemia can evolve to become life-threatening for a patient with diabetes.

A hyperglycemic crisis occurs when patients do not have sufficient circulating insulin. The form taken by the crisis depends on whether there is any circulating insulin at all. When there is a total lack of insulin, such as for type 1 diabetes patients who rely on insulin injections, a hyperglycemic crisis will take the form of diabetic ketoacidosis (DKA). DKA is characterized by hyperglycemia, metabolic acidosis, ketonemia, dehydration, and loss of electrolytes.

At the other end of the spectrum, when there is a relative lack of insulin, such as with type 2 diabetes, patients have enough circulating glucose to avoid metabolic acidosis and ketonemia, so a hyperglycemic crisis will take the form of hyperosmolar hyperglycemic state (HHS). HHS is characterized by hyperglycemia that can be twice as high as in DKA, plus dehydration and loss of electrolytes, only mild ketonemia and acidosis, and notable mental status changes or coma (Kitabachi et al., 2006).

Symptoms of both DKA and HHS can include dehydration, loose skin turgor, dry mucus membranes, tachycardia, deep slow breathing (Kussmaul respirations in diabetic ketoacidosis), hypotension, mental confusion, and possibly coma. The saying

“Cold and clammy, give ’em candy, but hot and dry, blood sugar is high.”

can be helpful to remember the symptoms between the two BG extremes. Lab tests should include plasma BG, ABGs, basic chemistry panel, ketones for blood and urine. Ketones will be positive in DKA but not always seen in HHS if the patient still has some endogenous insulin to prevent ketosis.

Case Scenarios of the Development of DKA and HHS

Compare these two scenarios in which an older woman living alone developed a hyperglycemic crisis.

Diabetic ketoacidosis

- The woman has type 2 diabetes and requires insulin.
- She gets pneumonia on Friday afternoon and develops a fever.
- Saturday morning she is tired and somewhat confused.
- She forgets to take her insulin all day Saturday.
- Sunday, she is found confused, breathing heavily, and having severe abdominal pain, and she is hospitalized with DKA.

Hyperosmolar hyperglycemic state

- The woman has undiagnosed type 2 diabetes.
- She gets pneumonia on Friday afternoon and develops a fever.
- Saturday morning she is tired and somewhat confused.
- She is too weak to eat and has only a cup of tea all day Saturday.
- Sunday, she is weaker, drinks a cup of tea, and eats a few crackers.
- Monday, she can barely get out of bed.
- Tuesday, she is found unconscious, and she is hospitalized with HHS.

In the hospital, hyperglycemic crises are treated aggressively. Intravenous fluids are given to replace the water deficit. Insulin is given to correct the hyperglycemia. Electrolytes are replaced as needed. Meanwhile, the cause of the crisis—usually an illness or injury—is treated. In a good hospital, DKA has a mortality rate of less than 5%, while HHS has a mortality rate of about 11% (Kitabachi et al., 2006). The reason for higher mortality in HHS is that often the patients are older and have more comorbidities, and the hyperglycemia went unrecognized before medical care could be given.

Test Your Knowledge

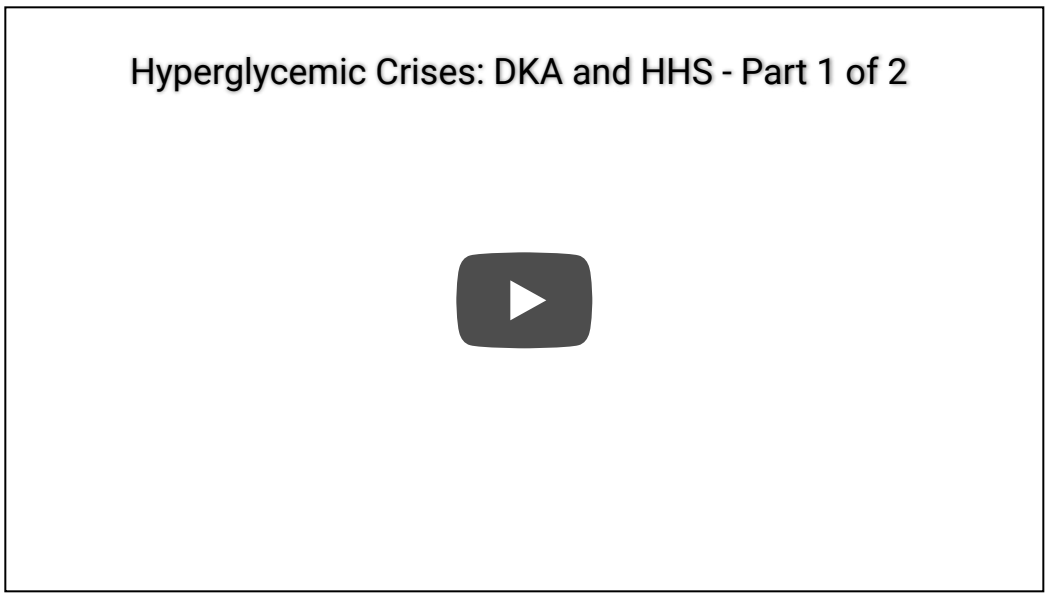
1. Ketones (ketone bodies) are:
   A. Large proteins leaked from the urine in diabetic kidney disease.
   B. Sugars that attach to proteins such as hemoglobin during long-term hyperglycemia.
   C. Small acidic molecules produced during starvation or when there is no insulin in the bloodstream.
   D. Complex carbohydrates that combine with cholesterol and then contribute to the formation of atherosclerotic plaque.

2. Hyperglycemic crises:
   A. Are treated with IV glucose.
   B. Can be treated in unconscious patients with a glucagon injection.
   C. Are treated with IV fluids and insulin.
   D. Are fatal >50% of the time, even in the best hospitals.

Apply Your Knowledge

What different lab values would you expect to see between DKA and HHS?

Video (14:53)



Difference between DKA and HNS, Parts 1 of 2
https://www.youtube.com/watch?v=-movg3ubceA

Both answers: C

Hypoglycemic Crises

Hypoglycemia occurs when a person's blood glucose is too low, usually below 70 mg/dl. People with hypoglycemia become pale, shaky, sweaty, weak, and hungry. If the hypoglycemia is prolonged, they will become confused and possibly comatose. Symptoms can often mimic intoxication and must be confirmed with a fingerstick BG to avoid misdiagnosing.

Causes of Hypoglycemia

Patients who have type 2 diabetes and who take insulin or insulin secretagogues, such as the sulfonylureas, can become hypoglycemic if:

- Too much insulin or secretagogue is taken
- The secretagogue was not discontinued when insulin was added
- Too few carbohydrates are eaten
- Circulating glucose is depleted too quickly (eg, during exercise)
- Alcohol intake occurs without eating
- Kidney disease exists

Source: Cryer, 2011.

The treatment for hypoglycemia in a conscious person is 15 to 20 g of oral glucose. The **Rule of 15** guides that patients with symptoms of "cold and clammy" should take a fingerstick BG. If the BG is < 60 mg/dL, 15 grams of a fast-acting sugar should be given (1/2 cup orange juice, 4–6 pieces of candy,1 cup of milk, 2 graham crackers). Check the blood sugar again in 15 minutes and, if it hasn't risen above 70 mg/dL, eat or drink another 15 grams of carbohydrate. Wait another 15 minutes and check a blood sugar again. If the blood sugar is still not above 70, call for medical help.

After blood sugar returns to normal, plan to eat a regular meal with protein within the next hour. Do not treat hypoglycemia with sugar-free sodas or chocolate candy with nuts. The chocolate may create a rebound hypoglycemia and the fat in nuts may slow the absorption of the sugar. Teaching patients to identify causes of hypoglycemia and to wear some form of identification is important to avoid future episodes.

Unconscious people can be given an intramuscular injection of glucagon (GlucaGen). In a hospital setting, an IV infusion or bolus of 50% dextrose may be given. Be careful when giving IV 50% dextrose because it is thick and can cause phlebitis or tissue necrosis.

Common Simple Carbohydrates (15 g)

15 grams of simple carbohydrates commonly available are:

1. Glucose tablets (follow package instructions)
2. Gel tube (follow package instructions)
3. 1 small box of raisins
4. 1/2 cup of juice or regular soda (not diet)
5. 1 tablespoon sugar, honey, or corn syrup
6. 8 ounces of nonfat or 1% milk
7. 6–7 small hard candies, such as Lifesavers

For their protection, all patients who have diabetes should be taught the symptoms of hypoglycemia. Also, after monitoring their blood glucose level for a few months, patients will learn to predict which situations will give a dip in their blood glucose concentration. Those with type 2 diabetes who tend to become hypoglycemic should carry glucose tablets, and if patients have a history of significant hypoglycemic episodes, their families, associates, or caretakers should know when and how to give an injection of glucagon (ADA, 2015).

Test Your Knowledge

Hypoglycemia

A. Should be treated with oral glucose in conscious patients.
B. Can only be treated with IV glucose if the patient is unconscious.
C. Should be treated with insulin injections in both conscious and unconscious patients.
D. Is a problem for people with type 1 diabetes but not for those with type 2 diabetes.

Apply Your Knowledge

What are some fast-acting sugars you can give a patient experiencing hypoglycemia?

Answer: A

Chronic Complications of T2DM

By identifying diabetes early many chronic complications can be avoided or minimized. Cardiovascular and microvascular complications may be prevented or delayed when glycemic levels are controlled. A hallmark study known as the Diabetes Control and Complications Trial (DCCT) revealed maintaining blood glucose levels to a near-normal level may significantly reduce chronic complications. The DCCT demonstrated in 1993, in the final report of the study, that microvascular complications could be significantly reduced up to 70% when glycemic goals are within near-normal levels (NIDDK, 2008).

Acute and significant changes in a person's blood glucose level can cause life-threatening problems. Slow, chronic hyperglycemia is the source of most diabetic illness and death. Longstanding hyperglycemia causes or worsens the following:

- **Atherosclerotic arterial disease**, leading to hypertension, myocardial infarction, renal vascular insufficiency, and stroke
- **Kidney damage** (diabetic nephropathy), leading to end-stage renal disease requiring dialysis or kidney transplant
- **Eye injury** (diabetic retinopathy), with macular edema, retinal hemorrhages, neovascularization, glaucoma, and cataracts, any of which can cause visual impairment or blindness
- **Nerve damage** (diabetic neuropathy): Peripheral nerve damage leads to injuries of the feet, while autonomic nerve damage weakens bowel/bladder control and/or causes sexual impotence.
- **Poor wound healing** and a risk for infections, which can lead to limb amputations (Maitra, 2009)

Cardiovascular Damage: Atherosclerosis

Cardiovascular disease is a leading cause of death among all people and 65% of people with diabetes die from heart disease and stroke (NDEP, 2015). Both insulin resistance and the chronic hyperglycemia of type 2 diabetes accelerate the development of atherosclerosis, a disease of large- and medium-size arteries. Atherosclerosis then causes myocardial infarctions, peripheral artery obstructive disease, renal artery disease, and strokes.

The ABCs of Diabetic Care

A—A1c (blood glucose) less than 7 percent

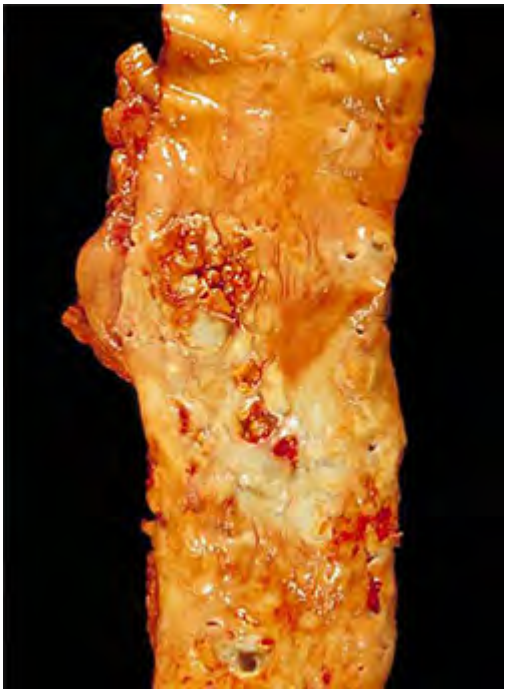
B—Blood pressure less than 130/80 mm Hg

C—Cholesterol, LDL less than 100 mg/dl

Atherosclerosis is a major problem in people with diabetes. Atherosclerotic artery disease is a hundred times more likely to cause gangrene of the lower limb in people with diabetes than in people without diabetes. Moreover, atherosclerotic myocardial infarctions are the most common cause of death in people with diabetes (Maitra, 2009). Deaths from cardiovascular disease are 4 times higher in people with diabetes than in other people. An educational focus to reduce illness and cardiovascular disease in people with diabetes is to focus on the ABCs of diabetes, as shown in the box below.

Atherosclerosis is only one of the detrimental cardiovascular consequences of diabetes. For example, people with diabetes tend to have poorer outcomes after ischemic heart injury, and people with diabetes are 2 to 5 times more likely than people without the disease to develop heart failure (Nesto, 2007).

Atherosclerosis of a Large Artery



The aorta has been slit lengthwise and laid open to show the extensive atherosclerosis of its walls. White fatty plaque and disrupted lesions cover the inner lining. Source: CDC, 1972.

Due to their increased cardiovascular risk, diabetic patients with symptoms suggesting coronary ischemia, especially substernal discomfort brought on by exercise and relieved by rest—should be given an exercise or non-stress ECG. If the test results are abnormal, the patient is referred to a cardiologist.

Management of Cardiovascular Disease

- Diabetic patients who have cardiovascular disease or who have an increased risk for the disease because of their age, family history, a history of smoking, or the presence of hypertension, dyslipidemia, or albuminuria, should be put on an antiplatelet therapy of 81–162 mg/day aspirin.
- Hypertension should be reduced to systolic pressure <130 mm Hg and diastolic pressure <80 mm Hg.
- Preferred medications are ACE inhibitors and angiotensin receptor blockers (ARBs), except in pregnant women.
- Lipid levels should be toward healthy ranges. The primary goal is to reduce LDL cholesterol <100 mg/dl, and statins should be considered.

Source: ADA, 2015.

Test Your Knowledge

Diabetic cardiovascular disease:

A. Usually appears as a bleeding disorder in which the patient's blood clots too slowly.
B. Is usually treated with bed rest and a much reduced level of physical activity.
C. Is usually the result of atherosclerosis.
D. Is uncommon but usually appears as micro hemorrhages in the skin.

Apply Your Knowledge

What pharmaceutical and lifestyle behaviors can help decrease overall cholesterol to recommended levels?

Answer: C

Renal Damage: Nephropathy

In the United States, diabetic kidney damage is the most common cause of end-stage renal disease. This type of kidney damage, **diabetic kidney disease (DKD)** or diabetic nephropathy, first appears as small amounts of albumin leaking into the urine (microalbuminuria). Without treatment, microalbuminuria progresses to a more significant leakage, macroalbuminuria. Progression from microalbuminuria to macroalbuminuria takes place within 10 to15 years in 20% to 40% of those with type 2 diabetes. Less than ten years afterwards, 20% of patients with macroalbuminuria will develop end-stage renal disease and will need dialysis or a kidney transplant. After myocardial infarction, renal failure is the largest killer of people with diabetes (Maitra, 2009).

Patients with type 2 diabetes should be regularly screened for microalbuminuria, beginning at the time of diagnosis (NKF-KDOQI, 2015). Diabetic retinopathy is often present by the time diabetic kidney disease appears, and albuminuria in a patient with diabetic retinopathy is most likely due to diabetic kidney disease. A serum creatinine level should also be measured yearly as a general assessment of kidney function (ADA, 2015).

Management of Diabetic Kidney Disease

- Improve glycemic control, with a goal of A1c <6.5%; intensive control of hyperglycemia can prevent DKD and may slow the progression of DKD if it already exists.
- Treat hypertension to a goal of <130/80 mm Hg using an ACE inhibitor or an ARB.
- If a patient already has micro- or macroalbuminuria, add an ACE inhibitor or an ARB regardless of the blood pressure (ADA, 2015).
- Reduce blood LDL cholesterol levels to <100 mg/dl and preferably to <70 mg/dl; if medication is needed, a statin is the drug of choice, except in patients on hemodialysis.
- Reduce daily protein intake to 0.8 g/kg of body weight in diabetic patients with chronic kidney disease; this will make proteins approximately 10% of their total daily calories.
- Reduce body weight to within the BMI range of 18.5 to 24.8 kg/m2.

Source: NKF-KDOQI, 2007.

Test Your Knowledge

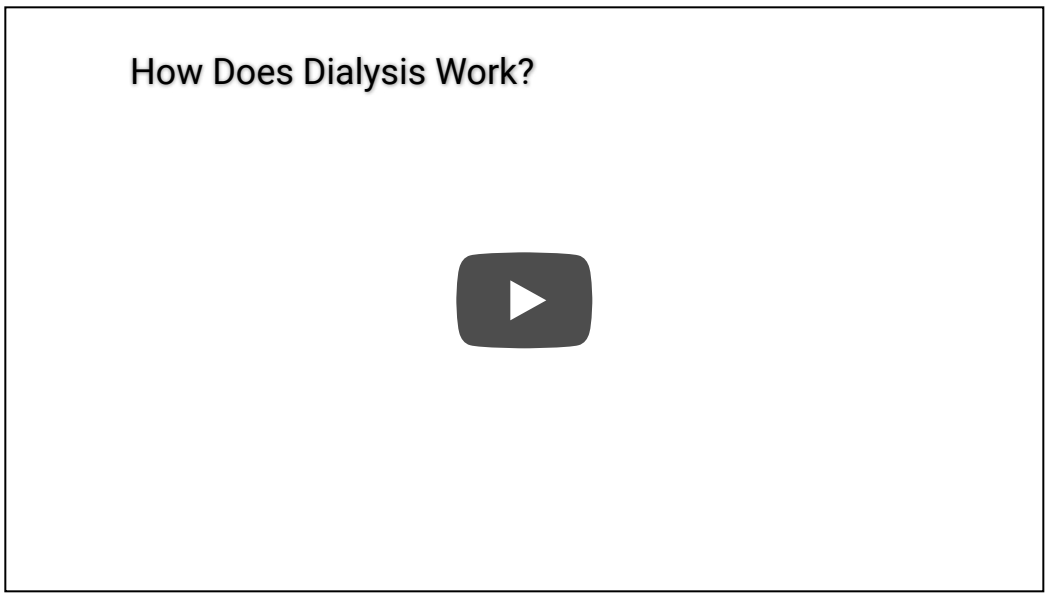
Diabetic kidney disease is:

A. Typically diagnosed by the presence of blood in the urine.
B. The most common cause of end-stage renal disease in the United States.
C. Typically diagnosed by the presence of glucose in the urine.
D. Also called diabetic neuropathy.

Apply Your Knowledge

What foods are included in a low-salt and low-protein diet for someone with chronic kidney disease?

Video (3:17)



https://www.youtube.com/watch?v=fKlY2SKi_dk

Answer: B

Ophthalmic Damage

Diabetes damages the eyes in a number of ways, including diabetic retinopathy, and the onset of cataracts and glaucoma.

Diabetic Retinopathy

Diabetes damages small blood vessels and capillaries throughout the body. Basement membranes are thickened, supportive cells are injured, and the blood vessels in the back of the retina may rupture and leak, exuding fluid and producing tiny hemorrhages. Diabetic retinopathy is a leading cause of new cases of legal blindness among adult Americans (AAO, 2016).

Patchy Vision Induced by Diabetic Retinopathy

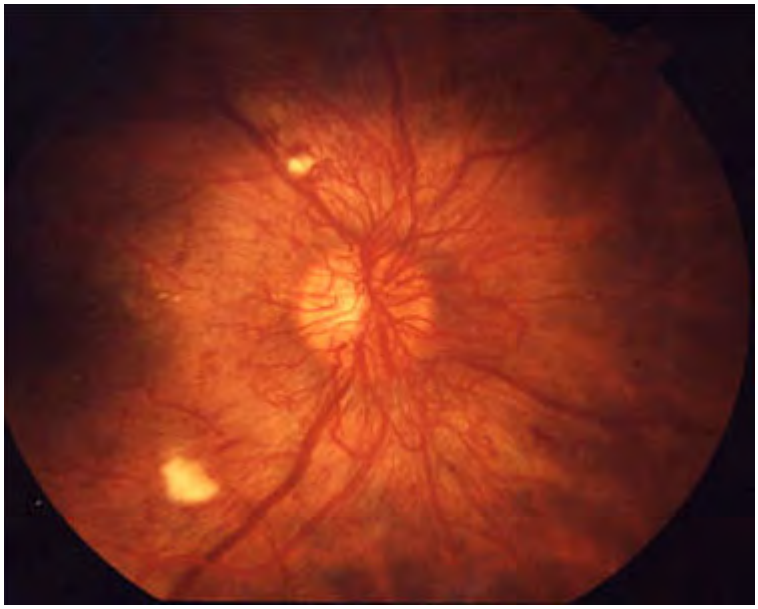
The picture on the right simulates the patchy vision that can be produced by diabetic retinopathy. Source: NWS, 2005.

In the retina, micro hemorrhages and fluid leakage first produce macular edema and lipid deposits (hard exudates), both of which can lead to decreased vision. The blood vessel damage also causes reduced perfusion, and this stimulates the second stage of diabetic retinopathy, called *proliferative* diabetic retinopathy. In proliferative diabetic retinopathy, new blood vessels grow along the surface of the retina, called *neovascularization*, causing web-like vessels that further disrupt the function of the retina and cause decreased vision (Folberg, 2009).

Cataracts and Glaucoma

Diabetes also increases a patient's chances of developing cataracts and glaucoma.

Neovascularization of the Retina



A funduscopic view of the optic disc of a person with diabetic retinopathy. Normally, about four large vessels would emerge from the optic disc. Here, a great many extra blood vessels grow across the optic disc and retina. Source: University of Michigan Kellogg Eye Center.

Management of Diabetic Retinopathy

- Chronic hyperglycemia causes rapid development of diabetic eye problems. Glycemic control, with a goal of A1c <6.5%, is a key to reducing the risk and slowing the progression of diabetic retinopathy.
- Hypertension is an additional risk factor, and blood pressure control, with a goal of <130/80, slows the progression of diabetic retinopathy.
- A high serum level of lipids makes a person with diabetes more likely to develop diabetic retinopathy. Serum LDL cholesterol should be reduced to <100 mg/dl and serum triglycerides should be reduced to <150 mg/dl.
- People with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes and annually.
- Patients with any degree of diabetic retinopathy should be referred to a specialized ophthalmologist, who may treat high-risk diabetic retinopathy with laser coagulation therapy.

Source: AAO, 2015.

Test Your Knowledge

Diabetic retinopathy:

A. Can cause edema of the macular area of the retina as well as the ingrowth of excess blood vessels.
B. Is a macrovascular complication of diabetes and results from atherosclerosis of the small retinal blood vessels.
C. Is exacerbated by low blood pressure and low blood levels of LDL cholesterol.
D. Cannot be treated or slowed and will inevitably lead to blindness.

Apply Your Knowledge

How can a patient with diabetes track all the guidelines of care for themselves?

Online Resource

National Eye Institute website Facts About Diabetes Eye Disease

Answer: A

Nerve Damage: Neuropathy

Diabetes damages the nervous system. The most common problem in people with type 2 diabetes is a symmetric peripheral neuropathy in which patients become less able to feel things with their hands and feet. Diabetic nerve damage begins at the tips of the longest nerves and slowly progresses to shorter and shorter nerves; therefore, sensation is first lost in the toes, then in the ankles, and later in the fingers (Anthony et al., 2009).

People with diabetes who have decreased sensation in their feet can be unaware of foot injuries and tend to suffer injuries that cannot heal without special care. To make matters worse, people with diabetes often have reduced circulation in their feet along with generalized poor wound healing. These conditions cause gangrene of the extremities 100 times as often as people without the disease.

Diabetic neuropathy is not limited to peripheral sensorimotor nerves. Autonomic nerves throughout the body can be damaged by chronic hyperglycemia and cause **diabetic autonomic neuropathy**, which affects organs involved with autonomic functions. Patients with diabetic autonomic neuropathy can have postural hypotension, incomplete bladder emptying, or sexual dysfunction. Specific symptoms of diabetic autonomic neuropathy include:

- A resting tachycardia of >100 bpm

- Orthostatic hypotension, in which systolic pressure falls >20 mm Hg when the patient stands from a sitting position
- Gastroparesis, in which the stomach empties slowly or not at all
- Constipation, or constipation alternating with diarrhea
- Incomplete bladder emptying, which can cause recurrent urinary tract infections
- Erectile dysfunction
- Poor vision at night
- Asymptomatic heart attack

Management of Diabetic Neuropathy

Patients with type 2 diabetes should annually have their feet and hands tested for sensitivity to pain, temperature, light touch, vibration, and proprioception.

Peripheral neuropathy should be explained to patients so they will take special care to guard against injuries. Glycemic control should be improved to a level of A1c <6.5%. Currently, there are no cures for diabetic neuropathy, but symptoms can be treated. For instance:

For pain

Tricyclic drugs, anticonvulsants, serotonin/norepinephrine uptake inhibitors, or substance P inhibitors

For gastroparesis

Diet change or prokinetic drugs (eg, metoclopramide, erythromycin)

For erectile dysfunction

Phosphodiesterase type 5 inhibitors (eg, sildenafil), intraurethral prostaglandins, or physical erection aids

Source: Ferrante, 2007; ADA, 2015.

Test Your Knowledge

Autonomic diabetic neuropathy:

A. Leads to difficulty sensing pain in the feet.
B. Is the cause of diabetic Alzheimer's disease.
C. Is a psychological result of depression.
D. Can cause a variety of symptoms, such as postural hypotension, incomplete bladder emptying, and sexual dysfunction.

Apply Your Knowledge

How would you explain diabetic peripheral and autonomic neuropathy to a patient with diabetes?

Online Resource

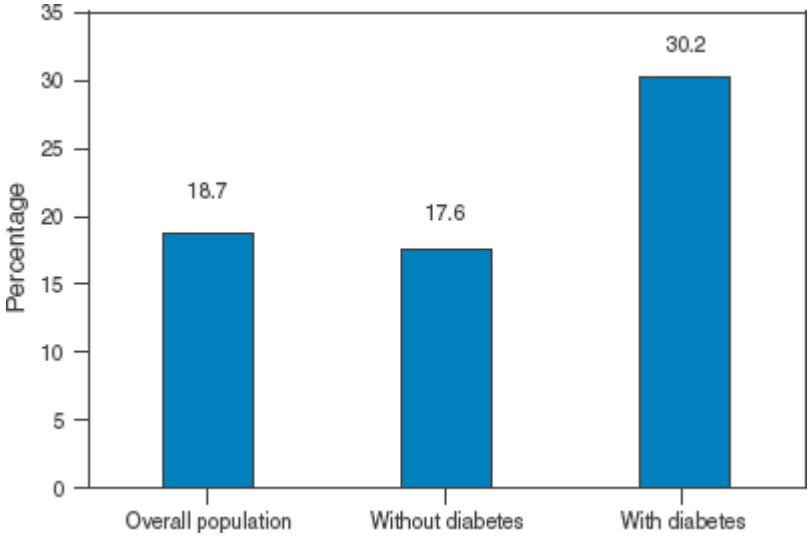
National Institute of Diabetes and Digestive and Kidney Diseases website: Diabetic Neuropathies: The Nerve Damage of Diabetes

Answer: D

Foot Damage

Normal daily activities are especially hard on feet and ankles, which support all of the body weight. In diabetes, feet and ankles lose sensation before other parts of the body. The loss of sensation means that people with diabetes lose the ability to adjust to changes in temperature, pressure, and position; therefore, they tend to injure and re-injure their feet and ankles more frequently and more severely than people without diabetes (ADA, 2012).

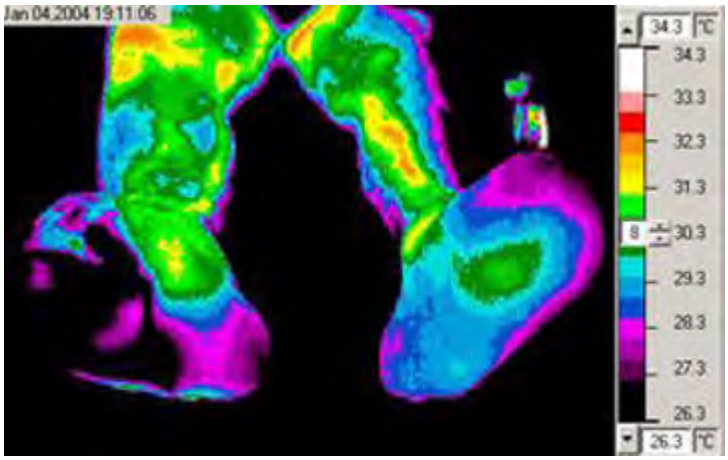
Lower Extremity Disease over Age 40



Percent of Americans ≥40 years old with lower extremity disease (ie, peripheral artery disease, peripheral neuropathy, foot ulcers, or lower extremity amputation). Lower extremity disease is almost twice as common in people with diabetes as in those without diabetes. Source: CDC.

As a further complication, people with diabetes have poorer perfusion of peripheral tissues than people without the disease.

Impaired Peripheral Perfusion in Diabetic Foot



Thermal imaging (heat-sensitive photography) shows that this patient's left foot is much cooler (the black regions) than the rest of his body, due to decreased peripheral circulation. (The patient is sitting and facing us.)
Source: NASA, 2009.

Wounds and skin infections heal poorly in persons with diabetes. In the United States, diabetes is the leading nontraumatic cause of lower limb amputations (Lipsky et al., 2004).

Management of Diabetic Foot Problems

Patients need annual foot exams, preferably by a diabetic foot specialist. The exam should:

- Inspect skin for abrasions, ulcers, nail infections, or calluses with underlying hemorrhage or discoloration.
- Look for tender areas, swelling, or deformities, such as contractures, joint hyperextension, flexures, and midfoot arthropathy (Charcot arthropathy)
- Test for sensory deficiencies using a tuning fork and a standard 10-g nylon monofilament.
- Test the ankle (Achilles tendon) reflex.
- Assess the perfusion of the foot, checking foot temperature, capillary refill in the toes, and strength of the foot pulses.
- Check shoes, because rubbing and inappropriate pressure points are common causes of foot ulcers.

Patients should be taught not to rely on sensation only, and they should examine their feet daily. They should choose their footwear carefully, keep their nails trimmed, and walk, run, and climb with extra caution.

Patients should be counseled to stop smoking.

Refer patients to foot care specialists for ongoing preventive care and life-long surveillance.

Teach patients with diabetes how to clean and care for their feet.

Source: Lipsky et al., 2004; Boulton et al., 2008; ADA, 2015.

Test Your Knowledge

Foot injuries in patients with diabetes:

A. Usually become gangrenous and lead to amputations.
B. Receive undue attention and are no more common than foot injuries in people without diabetes.
C. Are typically worsened by the increased peripheral circulation that results from hyperglycemia.
D. Can heal poorly and are more prone to infection than injuries in people without diabetes.

Apply Your Knowledge

How would you teach a patient with diabetes to check the bottom of their feet when they are obese and can't see their feet?

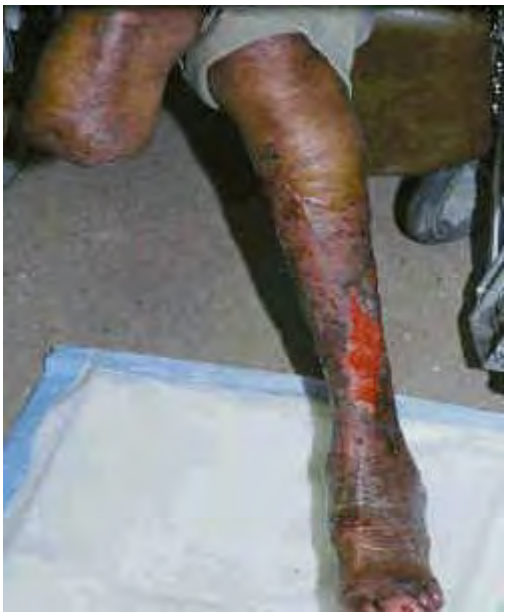
Answer: D

Integumentary Damage: Wounds and Infections

Infections are the cause of 5% of the deaths of patients with diabetes, who are especially prone to skin infections, pneumonia, and pyelonephritis. This heightened susceptibility to infection results from a number of factors (Maitra, 2009):

- Sluggish neutrophils with decreases in: chemotaxis, adherence to the endothelium, phagocytosis, and microbiocidal activity
- Decreased production of cytokines by macrophages
- Diminished or impaired local circulation, reducing delivery of oxygen, immune cells, and immune molecules to wounds
- Neuropathy, leading to unawareness of minor injuries
- Patient limitations, such as reduced vision

Poorly Healing Leg Ulcer in Patient with Previous Amputation



Source: NIDDK, 2007.

Management of Diabetic Wounds and Infections

- Prevention is the best "treatment" for diabetic infections. Patients should be taught about their neuropathies, how to daily inspect feet, how to purchase protective footwear, and how to care for their feet. They should also be taught that optimal glycemic control reduces their susceptibility to infections.
- Wounds and injuries should be reported to a member of the patient's diabetes team, and the clinician should then:
  - Consult a surgeon for severe wounds.
  - Clean and debride the wound.
  - Take a culture specimen.
  - Start antimicrobials if the wound appears clinically infected. Aerobic gram-positive cocci (typically, *Staphylococcus aureus* or beta-hemolytic streptococci) are the most common skin pathogens, but chronic wounds tend to have mixed infections that include gram-positive and gram-negative aerobes and anaerobes.
  - Initiate a diabetic wound care regimen.
  - Reassess progress daily for inpatients or in 2 to 5 days for outpatients.

With good care, mild to moderate infections should resolve in 80% to 90% of cases. Severe infections will resolve in 60% to 80% of cases.

Source: Lipsky et al., 2004; Baranoski & Ayello, 2008.

Test Your Knowledge

When caring for a wound in a person with diabetes:

A. Antimicrobial drugs should be begun if the wound looks infected, even before culture results are available to identify the microbes.
B. You should prepare the patient by warning them that most severe wounds will not heal.
C. Hospitalization and a surgical consult are mandatory for almost all wounds.
D. Contrary to wounds in healthier people, cleaning and debriding a diabetic wound increases the risk of infection.

Apply Your Knowledge

What products are available for wound care in PWD?

Online Resource

https://www.youtube.com/watch?v=yb1_E9cjV7M

Answer: A

Reproductive Damage: Male and Female

Chronic hyperglycemia impacts every body system, including the reproductive system. Reproductive health problems for men with diabetes include:

- Erectile dysfunction
- Androgen/testosterone deficiency
- Low libido (sexual desire)

- Retrograde ejaculation (semen flows back into the bladder)
- Balanitis (inflammation of the head of the penis)

Because normal erection depends on the ability of blood vessels to constrict correctly and respond neurologically, men with diabetes who have peripheral vascular disease and neuropathy are at risk for erectile dysfunction. Men with diabetes are three times more likely to have erectile dysfunction than men without diabetes.

Reproductive health problems for women with diabetes include:

- Low libido
- Gestational diabetes
- Fertility problems
- Menstrual irregularities
- Delayed menarche and early menopause
- Vaginal dryness and painful intercourse
- Absent orgasm (as many as 35% of women) (Zarzycki & Zieniewicz, 2005)

Assessment of sexual health needs to evaluated by clinicians and the diabetes team as this impacts quality of life. Careful and tactful questions can be asked, such as "Many people with diabetes have problems with sexual intimacy. How has it been for you? Do you have any concerns you'd like to discuss?" Referrals to psychologists for mental health issues that impact sexual relations may be appropriate. Medications such as tricyclic antidepressants may be needed to resolve sexual issues if the etiology is not physical. Support groups and resources should also be provided, and many are available online for use in the privacy of home.

Because the reproductive system in men involves the urinary tract system, urologic complications need to be assessed.

Psychological Damage: Depression

If you're tired of just reading about diabetes, imagine having to live with the chronic disease and not ever getting a break from it. Like any chronic disease, diabetes can last a lifetime and requires daily attention, which is exhausting. Diabetes burnout, stress, depression, denial, anxiety, and even anger are all issues that impact mental health for people with diabetes.

Assessment questions should be asked by the diabetes healthcare team to recognize and assess concerns and mental health disorders. Questions that are open ended and nonjudgmental can help patients feel free to discuss real concerns, such as "Many people with diabetes can feel sad or angry or have problems eating. How has it been for you?"

Studies show a relationship between new diagnosis of diabetes and depression. The mentally ill are also at a high risk of developing T2DM due to poor health maintenance, which can complicate blood glucose control and their mental illness. Referrals to advanced prepared psychologists and counseling may be needed. Support groups, online forums, and group education classes can be helpful resources.

Prevention of Type 2 Diabetes

People with prediabetes, people with components of metabolic syndrome, women who have had gestational diabetes, and people with a strong family history of diabetes are at risk for developing type 2 diabetes (Rosenzweig et al., 2008). With good clinical care and education, people with prediabetes can slow or prevent the progression to diabetes with a proactive regimen (ADA, 2015). The first step is recognizing prediabetes in people at risk.

Identifying People at Risk

National studies show that 1 in 3 adults have prediabetes and only 1 in 10 are aware of the diagnosis. Since 1997 the ADA has recognized the existence of levels of glucose elevation that are out of the normal range, but not yet at levels diagnostic for diabetes. These individual are at increased risk for the same target organ damage as those clinically diagnosed with diabetes. In contrast to newer guidelines that support use of the A1c in diagnosing diabetes, the newest American Association of Clinical Endocrinologists (AACE, 2016) recommend continued use of fasting plasma glucose or the 2-hour OGG to make the diagnosis of prediabetes. Newer ADA guidelines recognize A1c levels between 5.7% and 6.4% as being consistent with the diagnosis of prediabetes. Various professional groups recommend that the following people be screened for prediabetes at least every three years:

- All people >45 years old
- Women with a history of gestational diabetes or those delivering an infant >9 lb
- Adults with blood pressures of systolic >135 mm Hg or diastolic >80 mm Hg
- Adults with dyslipidemia
- People with a BMI >25
- People with a large waist circumference > 35 in

- People with a strong family history of diabetes (type 2 diabetes in a first- or second-degree relative)
- People of ethnic groups that are especially prone to diabetes: Native American, African American, Latino, Asian American, or Pacific Islander (USPSTF, 2008; ADA, 2015)

Proactive Management of Prediabetes

In partnership with the CDC, the diabetes prevention program (DPP) teaches people in a twelve-month program to implement lifestyle change. Studies have shown that those involved in the program lost weight and decreased their risk in developing diabetes.

People with prediabetes should lose weight, increase their physical activity, modify their diets by increasing dietary fiber, and reduce calories, saturated fats, and trans fats. A clinician may consider the addition of metformin as an adjunct to lifestyle changes. Additionally, patients should reduce their cardiovascular risk factors by reducing their blood pressure to below 130/80 mm Hg and correcting any dyslipidemia.

These interventions can be difficult for patients to follow for long periods. The most effective treatment regimens include frequent contact between patients and their diabetes team members. Prediabetes patients also need regular visits with their physician. Studies show that with proactive care the incidence of type 2 diabetes can be reduced by 40% to 50% (Guangwei et al., 2008).

Test Your Knowledge

Prevention of type 2 diabetes means:

A. Reversing insulin resistance with chromium supplements and antioxidants.
B. Slowing or stopping the progression of prediabetes to type 2 diabetes.
C. Giving insulin injections to people at risk for developing type 2 diabetes.
D. Treating chronic complications, such as diabetic kidney disease, before they begin.

Apply Your Knowledge

What can you do in your current professional role to advocate for decreasing prediabetes in your patients, and even yourself?

Answer: B

Summary

Type 2 is the most common form of diabetes mellitus. It is a disease in which insulin is not as effective as in healthy people, and therefore more circulating insulin (hyperinsulinemia) is needed to keep blood sugar levels within the normal levels. This increase in needed insulin creates insulin resistance.

Insulin resistance occurs when body cells don't allow glucose to enter easily and is worsened by overweight and physical inactivity. In addition to having insulin resistance, people with type 2 diabetes progressively lose the ability to produce insulin, as the beta cells in their pancreas gradually fail.

Both insulin resistance and beta cell failure worsen with time, so type 2 diabetes is usually a disease of middle-aged people; however, overweight and obese people of any age are at risk. A typical person with type 2 diabetes is overweight, physically inactive, and comes from a family with a history of diabetes or an ethnicity (African American, Hispanic/Latino, Native American, Asian American, or Pacific Islander) with a high risk for the disease.

Today, most people with type 2 diabetes are diagnosed from a screening blood test before the disease becomes clinically symptomatic. Diagnosis of diabetes mellitus is made by any one of these approved blood tests:

- A fasting plasma glucose level >126 mg/dl documented on two different days
- A random plasma glucose level >200 mg/dl along with classic symptoms of diabetes
- A 2-hour oral glucose-tolerance test >200 mg/dl after ingesting 75 g of glucose documented on two different days
- An A1c > 6.5% (ADA, 2015)

Chronic hyperglycemia damages tissues, and the primary goal of people with diabetes is to keep episodes of hyperglycemia to a minimum. Regulation of blood glucose levels is called glycemic control. In general, people with type 2 diabetes have three target measurements for their degree of glycemic control: their fasting blood glucose levels should be 70 to 130 mg/dl, their long-term average A1c value should be < 6.5% and postprandial BG should be <180 mg/dl.

The initial management approach in type 2 diabetes is to maintain good glycemic control by adjusting lifestyle behaviors; specifically, by losing weight, increasing physical activity, and eating a healthier diet. Later, most patients with type 2 diabetes need the help of oral medications to avoid chronic hyperglycemia. The first medication is generally recommended to be metformin. As the disease progresses and their beta cells fail, many people with type 2 diabetes eventually need supplemental insulin.

Diabetes puts people at risk for macrovascular problems, particularly atherosclerotic cardiovascular disease, with an increased chance of heart attacks and strokes; therefore, a key part of the management of diabetes is to reduce any additional cardiovascular risk factors. People with type 2 diabetes should keep their blood pressures low (<130/80 mm Hg), they should eat high-fiber, low-fat diets, and they should keep their blood lipids in a heart-healthy range.

In addition to cardiovascular problems, patients with diabetes are prone to microvascular problems that damage eyes, kidneys, and nerves. People with diabetes also suffer from poor wound healing. Maintaining good glycemic control and a low blood pressure will reduce the tissue damage caused by microvascular diabetic problems.

People with diabetes must take extra care to avoid injuries, especially to their feet. Wounds, infections, and injuries cause more hospitalizations than for people without diabetes, and wounds and infections need to be treated early and aggressively. When they are sick or hurt, people with diabetes should consult with their health team.

The statistics of diabetes show a growing percentage of people with diabetes, prediabetes, and metabolic syndrome. When a person is discovered to have prediabetes, the progression to type 2 diabetes can often be delayed with the same treatments that are used for T2DM. People with prediabetes and diabetes are all encouraged to lose between 5% and 10% of their total body weight, increase their physical activity, reduce their caloric intake, reduce the fat in their diet, and eat more dietary fiber. For some people with prediabetes, adding an anti-diabetic medication such as metformin is also helpful.

Disease Management in Brief

Diagnosis of prediabetes

- FPG = 100–125 mg/dl (impaired fasting glucose) on two separate occasions or
- 2-hour plasma glucose level (after a 75-g glucose load) = 140–199 mg/dl (impaired glucose-tolerance) on two separate occasions
- A1c between 5.5% and 6.4%

Diagnosis of diabetes (by any 1 test)

- FPG >126 mg/dl (on separate days)
- Random plasma glucose >200 mg/dl with symptoms
- 2-hour plasma glucose level (after a 75-g glucose load) >200 mg/dl (repeated on a separate day)
- A1c > 6.5 confirmed by repeating on a different day

Diabetes Treatment Goals

Blood glucose

- A1c 4 <6.5%
- FPG = 70–<130 mg/dl
- Peak PPG= <180 mg/dl

Blood pressure

- Systolic <130 mmHg
- Diastolic <80 mmHg

Lipid profile (fasting)

- LDL cholesterol <100 mg/dl (<70 mg/dl when cardiovascular disease is already present)
- HDL cholesterol: men >40 mg/dl, women >50 mg/dl
- Triglycerides <150 mg/dl

Followup schedule

- Each 3 to 6 months
- History: review diet, exercise, lifestyle, smoking, alcohol use
- Exam: check weight, blood pressure, feet, patient's psychological health
- Labs: check A1c, self-monitored glucose records
- Medicines: review medicines, consider low-dose aspirin to prevent CVD

Add to annual check-up

- Exam: calculate BMI
- Labs: check serum creatinine, urine albumin/creatinine ratio
- Medications: flu shot, ensure patient had pneumococcal vaccination

CVD = cardiovascular disease
FPG = fasting plasma glucose
PPG = postprandial glucose
Source: ADA, 2015.

Putting It All Together: Case Scenario

Samuel Gonzalez, as you remember from our introductory scenario, is a 58-year old Hispanic male who comes for an initial physical exam after complaining of constant thirst, fatigue, blurred vision, and decreased sensation in his feet for 6 months. At his wife's insistence, he hopes there is a pill he can take to stop the annoying symptoms. He is a construction worker and wants to feel better. He was told to bring labs before the physical exam.

Q: What is the information needed for the initial exam?
A: A thorough history can reveal risk factors and family history as risks for diabetes mellitus.

Q: What information should be obtained in the physical exam?
A: A thorough head to toe assessment should include an exam of all body systems, including the eyes for any indications of retinopathy, the feet to assess for poor healing wounds or changes in musculature. Because he has already indicated poor sensation in his feet, the clinician should test for neuropathy using a monofilament and tuning fork for sensation and vibration. All the classic vital signs of course are needed.

Samuel's chart reveals the following:

Biometrics

Height: 65 inches
Weight: 186 lbs (84 kg)
BMI: 30.9 (obese)

Vital signs

Pulse: 62 bpm
BP: 136/82 mm Hg
Sa02: 94%
T: 98.7
R: 20

Pertinent laboratory results

FPG: 179 mg/dL
Serum creatinine: 1.1 mg/dL
eGFR: 72 mL/min/1.73m2
LDL-C: 218 mg/dL
HDL 28
Total cholesterol 250 mg/dL

Medical history

Hypertension

Surgical history

Dental teeth extraction from abscess

Family history

Mother had large babies in Mexico
Father died from a heart attack and was a smoker

Social history

Married, with four children
Smoker
Alcohol use (1–2 beers after work daily)

Current medications

Lisinopril 20 mg once daily

Known drug allergies

None

Q: What is the probable diagnosis?
A: Type 2 Diabetes Mellitus.
Rationale: The FBS is >126 mg/dL, with symptoms

Q: What additional questions should the clinician ask Mr. Gonzalez?
A: Questions about erectile dysfunction, depression; desire for smoking cessation and DSME instruction should be pursued.

Mr. Gonzalez is not surprised to hear he has developed type 2 diabetes and admits that he has an older brother and uncle with T2DM. He said his wife does want him to stop smoking and he has tried on his own but can’t quit. He also admits to some instances of ED and just thought it was his age.

Q: What referrals and additional lab tests should be ordered?
A: He should be referred to an optometrist, a smoking cessation program, and certified diabetes educator for DSME. The clinician warns him to “stop smoking, lose weight, exercise, and don’t eat so much.” Because of his existing symptoms and risk factors, the physician also puts him on oral metformin 500 mg bid and oral simvastatin 40 mg qd, and oral bupropion (Zyban) 150 mg bid for smoking cessation. He is told to return in 3 months for a followup after his DSME. A plan is developed to address his ED and probable retinopathy and neuropathy in 3 months after his body has had time to adjust to the medications and the goal of smoking cessation.

A point-of care-office lab test for A1c is completed and the result is 10.8%. He is given a booklet on diabetes with online resources and a referral to the DSME program covered by his insurance company.

Q: At the first DSME meeting with the diabetes educator, what topics should be covered?
A: Depending on his insurance coverage and allowable hours, the diabetes educator should focus on teaching him how to use a glucometer and discuss meal planning improvements. Although there are seven self-care management strategies to be covered, beginning with key survival skills is important. Teaching him how to use a glucometer will allow him self-feedback on all other behavior modifications he attempts (eg, meal planning, exercise). Followup or class teaching visits could focus on teaching the seven DSME topics, avoiding complications, and involving his wife.

Q: What next steps would occur at the 3-month followup visit and thereafter?
A: The physician should review a recent cholesterol panel and an A1c to compare with the initial A1c and log book. Followup on blood pressure, smoking cessation, weight, progress with the DSME program, depression, and episodes of ED should be addressed. Followup visits for every 3 months during the first year would be appropriate, especially with acute problems. Annual exams would include, baseline ECG, fundoscopic eye exams, comprehensive lab work to measure liver and kidney function, a lipid panel, and encouragement to continue to see a dentist. Celebrating his progress and making him a partner with his medical goals are key to momentum toward positive lifestyle behaviors.

Resources and References

Resources

American Association of Diabetes Educators (AADE)

diabeteseducator.org
1 800 338 3633

American Diabetes Association

http://www.diabetes.org/
1-800-DIABETES (1 800 342 2383)

CDC Native Diabetes Wellness Program

www.cdc.gov/diabetes/projects/diabetes-wellness.htm

National Diabetes Education Program

www.ndep.nih.gov; www.yourdiabetesinfo.org
1 888 693-NDEP (1 888 693 6337)

National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK-NIH)

http://www2.niddk.nih.gov/

References

Abraham T, Fox C. (2013, August). Implications of rising prediabetes prevalence. *Diabetes Care* 36(8):2139–41. Retrieved February 20, 2016 from http://care.diabetesjournals.org/content/36/8/2139.full.

Aguilar M, Bhuket T, Torres S, et al. (2015). Prevalence of the metabolic syndrome in the United States, 2003–2012. *JAMA* 313(19):1973–74. doi:10.1001/jama.2015.4260. Retrieved February 20, 2016 from http://www.diabetes.org/diabetes-basics/statistics/.

Ahmed, A. (2002). History of Diabetes Mellitus. *Saudi Medical Journal* 23(4):373–78.

American Academy of Ophthalmology (AAO). (2016). Diabetic Retinopathy. Preferred Practice Pattern Guidelines. Retrieved from http://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2016.

American Association of Clinical Endocrinologists (AACE). (2011, Mar/Apr). Medical Guidelines for Clinical Practice for Developing a Diabetes Mellitus Comprehensive Care Plan. In Handelsman Y, et al., *Endocrine Practice* 17(suppl 2).

American Diabetes Association (ADA). (2015). Diagnosis and classification of diabetes mellitus. *Diabetes Care.* Retrieved February 20, 2016 from http://www.diabetes.org/diabetes-basics/statistics/.

American Diabetes Association (ADA). (2014). Diabetes Statistics. Retrieved February 20, 2016 from http://care.diabetesjournals.org/content/suppl/2014/12/23/38.Supplement_1.DC1/January_Supplement_Combined_Final.6-99.pdf.

American Diabetes Association (ADA). (2012). The Cost of Diabetes. Retrieved February 21, 2016 from http://www.diabetes.org/advocacy/news-events/cost-of-diabetes.html.

American Dietetic Association (Amer. Diet. Assoc.). (2015). Position of the American Dietetic Association: Health implications of dietary fiber. *Journal of the American Dietetic Association* 108(10):1716–31.

Anthony DC, Frosch MP, de Girolami U. (2009) Peripheral nerve and skeletal muscle. In V Kumar, AK Abbas, N Fausto, and JC Aster (eds.), *Robbins and Cotran: Pathologic Basis of Disease*, 8th ed. Philadelphia: Elsevier, Ch. 27.

Basu A, et al. (2009). Effects of type 2 diabetes on insulin secretion, insulin action, glucose effectiveness, and postprandial glucose metabolism. *Diabetes Care* 32(5): 866–73.

Baranoski S, Ayello E. (2008). Wound Care Essentials: Practice Principles. Baltimore: Wolters Kluwer, Lippincott Williams & Wilkins.

Bolen S, et al. (2007). Comparative effectiveness and safety of oral diabetes medications for adults with type 2 diabetes. Comparative Effectiveness Review. No. 8. AHRQ Publication No. 07-EHC010-EF (July 2007). Retrieved from http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=6&DocID=40.

Boulton AJM, et al. (2008). Comprehensive foot examination and risk assessment. A report of the Task Force of the Foot Care Interest Group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. *Diabetes Care* 31(8):1679–85. Retrieved from http://care.diabetesjournals.org/content/31/8/1679.full.

Buse JB, Polonsky KS, Burant CF. (2008). Type 2 diabetes mellitus. In HM Kronenberg, S Melmed, KS Polonsky, and PR Larsen (eds.), *Williams Textbook of Endocrinology*, 11th ed. Philadelphia: Saunders, Ch. 30.

Centers for Disease Control and Prevention (CDC). (2015). Prediabetes. Retrieved http://www.cdc.gov/diabetes/basics/prediabetes.html.

Centers for Disease Control and Prevention (CDC). (2014). National Diabetes Fact Sheet. Retrieved from http://www.cdc.gov/diabetes/data/statistics/2014statisticsreport.html.

Centers for Disease Control and Prevention. Diabetes National Diabetes Prevention Program (2012). Retrieved http://www.cdc.gov/diabetes/prevention/lifestyle-program/curriculum.html.

Centers for Disease Control and Prevention (CDC). (2013). Obesity in U.S. Adults, BRFSS, 2007. Retrieved from http://www.cdc.gov/nchs/data/databriefs/db131.htm.

Centers for Disease Control and Prevention (CDC). (2005). Quick stats: Lower extremity disease. *MMWR* 54(13):332. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5413a4.htm.

Centers for Disease Control and Prevention (CDC). (1972). CDC Public Health Image Library. Atherosclerosis, image ID #846 (Dr. Edwin P. Ewing, Jr.). Retrieved August 20, 2009 from http://phil.cdc.gov/Phil/home.asp.

Cernea S, Raz I. (2011). Therapy in the Early Stage: Incretins. American Diabetes Association. *Diabetes Care* 34(supp 2):S264–71 doi: 10.2337/dc11-s223. Retrieved from http://care.diabetesjournals.org/content/34/Supplement_2/S264.full.

Cryer PE. (2011). Hypoglycemia. In HM Kronenberg, S Melmed, KS Polonsky, and PR Larsen (eds.), *Williams Textbook of Endocrinology*, 12th ed. Philadelphia: Saunders, pp. 1552–77.

Diabetes Prevention Program Research Group (2009). Knowler W, et al. 10-year followup of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet* 374(9702):1677–86. doi: 10.1016/S0140-6736(09)61457-4. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135022.

Drucker D. (2008). Gastrointestinal hormones and gut endocrine tumors. In HM Kronenberg, S Melmed, KS Polonsky, and PR Larsen (eds.), *Williams Textbook of Endocrinology,* 13th ed. Philadelphia: Saunders, Ch. 38.

Drucker D, Nauck M. (2006). The incretin system: Glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. *Lancet* 368(9548):1696–1705.

Ebbell B. (1937). *The Papyrus Ebers, p. 115.* Copenhagen and Oxford: Oxford University Press.

Encyclopaedia Britannica. (1911). Diabetes. *Encyclopaedia Britannica,* 11th ed. 8: 145–46.

Ferrante M. (2007). Endogenous metabolic disorders. In CG Goetz (ed.), *Textbook of Clinical Neurology,* 3rd ed. Philadelphia: Saunders, Ch. 38.

Food and Drug Administration (FDA). (2015). Diabetes Prevention. Retrieved February 20, 2016 from http://www.fda.gov/ForPatients/Illness/Diabetes/ucm408100.htm.

Food and Drug Administration (FDA). (2011). Lantus (insulin glargine). Retrieved from http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm170089.htm.

Food and Drug Administration (FDA). (2008). Byetta (exenatide). Retrieved May 5, 2016 from http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm079781.htm.

Folberg R. (2009). The eye. In V Kumar, AK Abbas, N Fausto, and JC Aster (eds.), *Robbins and Cotran: Pathologic Basis of Disease*, 8th ed. Philadelphia: Elsevier, Ch. 29.

Funnell, M., et al. (2007). National standards for diabetes self-management education. *Diabetes Care* 30(6):1630–37.

Garber A, et al. (2008). Diagnosis and management of prediabetes in the continuum of hyperglycemia. When do the risks of diabetes begin? A consensus statement from the American College of Endocrinology and the American Association of Clinical Endocrinologists. *Endocrine Practice* 14(7):933–46.

Grant, R., Moore, A., Florez, J. (2009). Genetic architecture of type 2 diabetes: Recent progress and clinical implications. *Diabetes Care* 32(6):1107–15.

Guangwei L, et al. (2008). The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: A 20-year followup study. *Lancet* 371:1783–89.

Huether S, McCance K. (2012). Understanding Pathophysiology, 6th ed. Atlanta: Elsevier.

Jenkins N, et al. (2010). Initiating insulin as a part of Treat-to-Target in Type 2 diabetes (4-T) Trial: An interview study of patients' and health professionals' experiences. *Diabetes Care* 33(10) 2178–80.

Joffe D, Yanagisawa R. (2007). Metabolic syndrome and type 2 diabetes: Can we stop the weight gain with diabetes? *Medical Clinics of North America* 91(6):1107–23.

Kent D, d'Eramo G, Stuart P, et al. (2013). Reducing the risks of diabetes complications through diabetes self-management education and support. *Population Health Management* 16(2):74–81.

Kitabachi A, Umpierrez G, Murphy M, Kreisberg R. (2006). Hyperglycemic crises in adult patients with diabetes. A consensus statement from the American Diabetes Association. *Diabetes Care* 29(12):2739–48. Retrieved from http://care.diabetesjournals.org/content/29/12/2739.full.

Lipsky B, et al. (2004). Infectious Diseases Society of America Guidelines: Diagnosis and treatment of diabetic foot infections. *Clinical Infectious Diseases* 38: 885–910. Retrieved from http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Diabetic%20Foot%20Infection.pdf.

Maitra A. (2009). The endocrine system. In V Kumar, AK Abbas, N Fausto, and JC Aster (eds.), *Robbins and Cotran: Pathologic Basis of Disease*, 9th ed. Philadelphia: Elsevier.

Miller K, Beck R, Bergenstal R, et al. (2013). Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D exchange clinic registry participants. American Diabetes Association. *Diabetes Care* 36(7). Doi:10.2337/dc12-1770. Retrieved from http://care.diabetesjournals.org/content/36/7/2009.short.

Moghissi E, et al. (2009). American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care* 32(6):1119–31. Concurrently printed in *Endocrine Practice* 15(4):353–69.

Monnier L, Colette C, Owens D. (2009). Integrating glycaemic variability in the glycaemic disorders of type 2 diabetes: A move towards a unified glucose tetrad concept. *Diabetes/Metabolism Research and Reviews* 25(12):393–402. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19437415.

National Aeronautics and Space Administration (NASA). (2009). RST: Remote Sensing Technology, by Dr. Nicholas M. Short, Sr. Retrieved May 5, 2016 from http://rst.gsfc.nasa.gov/Intro/Part2_26d.html.

National Diabetes Education Program (NDEP). (2015).Changing the Way Diabetes is Treated. Retrieved from http://www.niddk.nih.gov/health-information/health-communication-programs/ndep/about-ndep/15th-anniversary/Documents/NDEP_15th_year.pdf.

National Diabetes Education Program (NDEP). (2014). *Diabetes,* the Statistics. Retrieved May 5, 2016 from http://www.niddk.nih.gov/health-information/health-statistics/Pages/default.aspx#category=diabetes.

National Eye Institute, NIH (NEI). (2016). *Photos, Images, and Videos.* Retrieved from https://nei.nih.gov/rop/photos.

National Diabetes Education Program (NDEP). (2015). The Link Between Diabetes and Cardiovascular Disease. Retrieved from http://ndep.nih.gov/media/CVD_FactSheet.pdf.

National Heart, Lung, and Blood Institute, NIH (NHLBI). (2000). The Practical Guide identification, evaluation, and treatment of overweight and obesity in adults. Retrieved http://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf.

National Institute of Diabetes and Digestive and Kidney Diseases, (NIH) (2008). Continuous Glucose Monitoring. Retrieved from http://www.niddk.nih.gov/health-information/health-topics/Diabetes/continuous-glucose-monitoring/Pages/index.aspx.

National Institute of Diabetes and Digestive and Kidney Diseases, NIH (NIDDK). (2016). *Diabetes Dictionary.* Retrieved from http://diabetes.niddk.nih.gov/dm/pubs/dictionary/index.htm.

National Institute of Diabetes and Digestive and Kidney Diseases, NIH (NIDDK). (2008a). National Diabetes Statistics, 2007. Retrieved from http://diabetes.niddk.nih.gov/dm/pubs/control/.

National Institute of Diabetes and Digestive and Kidney Diseases, NIH (NIDDK). (2008b). The Diabetes Control and Complications Trial and Follow-up Study. NIH Publication No. 08-3874. Retrieved from http://www.niddk.nih.gov/about-niddk/research-areas/diabetes/dcct-edic-diabetes-control-complications-trial-follow-up-study/Pages/default.aspx.

National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (NKF-KDOQI). (2007). KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. *American Journal of Kidney Diseases* 49(Suppl2): S12–S54.

National Weather Service, NOAA (NWS). (2005). Impairments to vision. Retrieved from http://www.nws.noaa.gov/sec508/htm/blindness.htm.

Nesto R. (2007). Diabetes and heart disease. In P Libby et al. (eds.), *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 10th ed. Philadelphia: Saunders.

O'Connor J, Johnson D, Freund G. (2006). Psychoneuroimmune implications of type 2 diabetes. *Neurologic Clinics* 24(3):539–59.

Pratt J. (1954). A reappraisal of researchers leading to the discovery of insulin. *Journal of History of Medicine* 9:281–89.

Strine T, Okoro C, Chapma D, et al. (2005). The impact of formal diabetes education on the preventive health practices and behaviors of persons with type 2 diabetes. *Preventative Medicine* 41(1):79–84.

Triplitt C. (2014). *Pharmacotherapy*, 9th ed. New York: McGraw Hill. Also published in *Diabetes Care* 2003;26(3):881–85.

UK Prospective Diabetes Study Group. (1998). Tight blood pressure control and risk of microvascular and macrovascular complications in type 2 diabetes. UKPDS 38. *British Medical Journal* 318(7175):29. Retrieved from www.ncbi.nlm.nih.gov/pubmed/9732337.

U.S. Preventive Services Task Force (USPSTF). (2008). Clinical Guidelines. Screening for type 2 diabetes in adults: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine* 148(11):846–54.

Mensing C. (ed). (2014). The Art and Science of Diabetes Self-Management Education, Desk Reference, 3rd ed. Chicago: AADE.

Wikipedia. (2012a). Glycogen. Retrieved May 5, 2016 from http://en.wikipedia.org/wiki/Glycogen.

Wikipedia. (2012b). Glucagon. Retrieved May 19, 2013 from http://en.wikipedia.org/wiki/Glucagon.

Wild S, Roglic G, Green A, et al.. (2004, May). *Diabetes Care* 27(5): 1047–53. Retrieved February 20, 2016 from http://care.diabetesjournals.org/content/27/5/1047.abstract.

Zarzycki W, Zieniewicz M. (2005, December). Reproductive disturbances in type 1 diabetic women. *Neuro Endocrinology* 26(6):733-38.

Post Test (Diabetes Type 2, 174)

Use the answer sheet following the test to record your answers.

1. The symptoms of diabetes mellitus were first identified:

    a. in 1921 by Canadian scientists Banting and Best.
    b. by European physicians around World War I.
    c. by early Egyptians and Ayurvedic healers over 3000 years ago.
    d. by the American Diabetes Association in 1960.

2. A 34-year old female patient presents with a symptoms of polyuria for 1 month and weight loss. Which diagnostic test is appropriate to diagnose this patient?:

    a. FBS on one occasion
    b. A1c
    c. 2-hour post prandial
    d. Random BG with symptoms

3. Glycogen is:

    a. A hormone produced in the pancreas.
    b. A polysaccharide that is stored in the liver.
    c. Produced in the striated muscles when exercising.
    d. An energy reserve that is slow to mobilize in an emergency.

4. Insulin:

    a. Is only available by injection or orally to treat T2DM.
    b. Is a hormone that acts on the liver to convert excess glucose into glycogen.
    c. Inhibits the uptake and use of glucose by skeletal muscles.
    d. Is manufactured and secreted by the alpha cells of the pancreas.

5. Glucagon:

    a. Is a peptide hormone that is stored in the pancreas.
    b. Is used to treat hyperglycemia by increasing the uptake of glucose in muscles.
    c. Is a hormone that acts on the liver to convert glycogen back into glucose.
    d. Stimulates the production of insulin.

6. People with type 2 diabetes have:

a. Insulin sensitivity, which is an over-reaction of cells to insulin.
b. No beta cells in their pancreas and no circulating insulin at all.
c. Chronic hypoglycemia.
d. Insulin resistance, which is a decreased response of cells to insulin.

7. In type 2 diabetes:

a. Beta cells in the pancreas cannot compensate for insulin resistance.
b. The pancreas is attacked by the body's immune system, resulting in pancreatitis.
c. The liver becomes overly sensitive to insulin.
d. Glucose cannot be used as fuel by any cells in the body.

8. Type 2 diabetes:

a. Is an inevitable disease of aging.
b. Is inevitable in people whose families have the disease.
c. May develop in genetically predisposed people with additional risk factors.
d. Is usually caused by the mutation of a single gene called T2D.

9. A health problem that directly increases the risk of developing type 2 diabetes is:

a. Intra-abdominal obesity.
b. Periodontal disease.
c. Foot injuries.
d. Osteoporosis.

10. The classic triad of symptoms of diabetes is:

a. Gluconeogenesis, glycosuria, and glycolysis.
b. Blurry vision, dehydration, and mental status changes.
c. Macular edema, albuminuria, and seizures.
d. Polyuria, polydipsia, and weight loss.

11. Prediabetes:

a. Is diagnosed when the fasting blood glucose level is >126 mg/dl.
b. Usually precedes type 2 diabetes.

c. Presents with the same triad of symptoms the same triad as diabetes.

d. Is not a threat to patients and need not be treated.

12. Metabolic syndrome:

a. Is an autoimmune disease.

b. Is no longer accepted as a medical term.

c. Is a cluster of components that must be treated individually.

d. Is a single disorder that puts a person at risk for psoriasis.

13. An A1c is the:

a. Typical fasting glucose level during the past few months.

b. Blood glucose level 2 hours after ingesting 75 g of glucose.

c. Average level of blood glucose over the past three months.

d. Blood glucose level after ≥8 hours of no caloric intake.

14. Of the oral anti-diabetic medications:

a. Insulin tablets are usually first to be added to a regimen of therapeutic lifestyle interventions.

b. Metformin is usually the first to be added to a regimen of therapeutic lifestyle interventions.

c. The second-generation sulfonylureas (glimepiride, glipizide, glyburide) are no longer prescribed.

d. Secretagogues are considered too risky to be used outside of a hospital setting.

15. Cardiovascular disease (CVD) is such a serious threat to people with type 2 diabetes that a patient should generally be given a lipid-lowering drug (a statin) if the patient has:

a. Type 2 diabetes and another risk factor for CVD, such as hypertension or abdominal obesity.

b. Type 2 diabetes and a family history of type 2 diabetes.

c. Prediabetes.

d. Prediabetes and a family history of type 2 diabetes.

16. In patients with type 2 diabetes, high blood pressure is:

a. Uncommon, being found in <25% of those with diabetes.

b. Typically treated using insulin supplements.

c. The most common cause of death (as listed on death certificates).

d. Considered to be ≥130/80 mm Hg.

17. People diagnosed with type 2 diabetes should get:

a. A rubella vaccination booster.

b. A tetanus vaccination booster.

c. Yearly influenza vaccinations.

d. Yearly pneumococcal polysaccharide vaccinations.

18. Ketones (ketone bodies) are:

a. Large proteins leaked from the urine in diabetic kidney disease.

b. Sugars that attach to proteins such as hemoglobin during long-term hyperglycemia.

c. Small acidic molecules produced during starvation or when there is no insulin in the bloodstream.

d. Complex carbohydrates that combine with cholesterol and then contribute to the formation of atherosclerotic plaque.

19. Hyperglycemic crises:

a. Are treated with IV glucose.

b. Can be treated in unconscious patients with a glucagon injection.

c. Are treated with IV fluids and insulin.

d. Are fatal >50% of the time, even in the best hospitals.

20. Hypoglycemia:

a. Should be treated with oral glucose in conscious patients.

b. Can only be treated with IV glucose if the patient is unconscious.

c. Should be treated with insulin injections in both conscious and unconscious patients.

d. Is a problem for people with type 1 diabetes but not for those with type 2 diabetes.

21. Diabetic cardiovascular disease:

a. Usually appears as a bleeding disorder in which the patient's blood clots too slowly.

b. Is usually treated with bed rest and a much reduced level of physical activity.

c. Is usually the result of atherosclerosis.

d. Is uncommon but usually appears as micro hemorrhages in the skin.

22. Diabetic kidney disease is:

a. Typically diagnosed by the presence of blood in the urine.

b. The most common cause of end-stage renal disease in the United States.

c. Typically diagnosed by the presence of glucose in the urine.

d. Also called diabetic neuropathy.

23. Diabetic retinopathy:

a. Can cause edema of the macular area of the retina as well as the ingrowth of excess blood vessels.

b. Is a macrovascular complication of diabetes and results from atherosclerosis of the small retinal blood vessels.

c. Is exacerbated by low blood pressure and low blood levels of LDL cholesterol.

d. Cannot be treated or slowed and will inevitably lead to blindness.

24. Autonomic diabetic neuropathy:

a. Leads to difficulty sensing pain in the feet.

b. Is the cause of diabetic Alzheimer's disease.

c. Is a psychological result of depression.

d. Can cause a variety of symptoms, such as postural hypotension, incomplete bladder emptying, and sexual dysfunction.

25. Prevention of type 2 diabetes means:

a. Reversing insulin resistance with chromium supplements and antioxidants.

b. Slowing or stopping the progression of prediabetes to type 2 diabetes.

c. Giving insulin injections to people at risk for developing type 2 diabetes.

d. Treating chronic complications, such as diabetic kidney disease, before they begin.

Answer Sheet

Diabetes Type 2: Nothing Sweet About It (174)

Name (Please print your name): _____

Date: _____

Passing score is 80%

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
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18. _____
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20. _____
21. _____
22. _____

23. _____

24. _____

25. _____

Course Evaluation (Diabetes Type 2, 174)

Please use this scale for your course evaluation. Items with asterisks * are required.

- 5 = Strongly agree
- 4 = Agree
- 3 = Neutral
- 2 = Disagree
- 1 = Strongly disagree

* Upon completion of the course, I was able to:

a. Summarize the history of Diabetes Mellitus.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

b. Summarize the prevalence, mortality, and morbidity of diabetes.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

c. Compare and contrast the four classifications of diabetes mellitus.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

d. Explain the body's regulation of blood glucose during the normal metabolism of foods and the pathology that arises with diabetes mellitus.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

e. Describe risk factors for diabetes mellitus.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

f. Explain the diagnostic criteria for diabetes mellitus.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

g. Identify risk factors for metabolic syndrome and prediabetes.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

h. Describe the optimal diabetes healthcare team and how they teach self-management.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

i. Explain treatment strategies for diabetes.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

j. Compare and contrast the acute and chronic complications of type 2 diabetes.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

k. Discuss the chronic complications of type 2 diabetes.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

l. Explain the two prongs of type 2 diabetes prevention.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* The author(s) are knowledgeable about the subject matter.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* The author(s) cited evidence that supported the material presented.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* This course contained no discriminatory or prejudicial language.

○ Yes ○ No

* The course was free of commercial bias and product promotion.

○ Yes ○ No

* As a result of what you have learned, do you intend to make any changes in your practice?

○ Yes ○ No

If you answered Yes above, what changes do you intend to make? If you answered No, please explain why.

* Do you intend to return to ATrain for your ongoing CE needs?

○ Yes, within the next 30 days.

- ○ Yes, during my next renewal cycle.
- ○ Maybe, not sure.
- ○ No, I only needed this one course.

* Would you recommend ATrain Education to a friend, co-worker, or colleague?

- ○ Yes, definitely.
- ○ Possibly.
- ○ No, not at this time.

* What is your overall satsfaction with this learning activity?

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* Navigating the ATrain Education website was:

- ○ Easy.
- ○ Somewhat easy.
- ○ Not at all easy.

* How long did it take you to complete this course, posttest, and course evaluation?

- ○ 60 minutes (or more) per contact hour
- ○ 50-59 minutes per contact hour
- ○ 40-49 minutes per contact hour
- ○ 30-39 minutes per contact hour
- ○ Less than 30 minutes per contact hour

I heard about ATrain Education from:

- ○ Government or Department of Health website.
- ○ State board or professional association.

- ○ Searching the Internet.
- ○ A friend.
- ○ An advertisement.
- ○ I am a returning customer.
- ○ My employer.
- ○ Other
- ○ Social Media (FB, Twitter, LinkedIn, etc)

Please let us know your age group to help us meet your professional needs.

- ○ 18 to 30
- ○ 31 to 45
- ○ 46+

I completed this course on:

- ○ My own or a friend's computer.
- ○ A computer at work.
- ○ A library computer.
- ○ A tablet.
- ○ A cellphone.
- ○ A paper copy of the course.

Please enter your comments or suggestions here: _____

_____

_____

_____

Registration Form (Diabetes Types 2, 174)

Please print and answer all of the following questions (* required).

* Name: _____

* Email: _____

* Address: _____

* City: _____ * State: _____ * Zip: _____

* Country: _____

* Phone: _____

* Professional Credentials/Designations:

_____

* License Number and State: _____

* Please email my certificate:

○ Yes ○ No

(If you request an email certificate we will not send a copy of the certificate by US Mail.)

Payment Options

You may pay by credit card or by check.
Fill out this section only if you are **paying by credit card.**
7 contact hours: $39

Credit card information

* Name: _____

Address (if different from above): _____

* City: _____ * State: _____ * Zip: _____

* Card type:

○ Visa ○ Master Card ○ American Express ○ Discover

* Card number: _____

* CVS#: _____

* Expiration date: _____