DIABETES RECOVERY GUIDE

THE ULTIMATE GUIDE TO TYPE II DIABETES

Thanks for choosing the *Diabetes Recovery Guide*, your one-stop source for all things diabetes. You're about to lay eyes on some priceless blood-sugar balancing tips and info, and we can't wait for you to use it to start fighting your diabetes naturally!

Before you go on, take a look at this special FREE video presentation, which reveals to you the "2 Deadliest Diabetes Lies"

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This eBook contains information that is intended as general advice to help the readers become better-informed consumers of health care.

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This book is not intended to be a substitute for the medical advice of a licensed physician. The reader should consult with his/her doctor about any matters relating to his/her health.

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Acknowledgements

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- Dr Raj, MD, a medical doctor with a specialization in pharmacology
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- Stone M., BA, a journalist with more than a dozen years of experience working in print journalism

Also acknowledged are the invaluable contributions of experts from the fields of biochemistry, nutrition, and physiotherapy.

Contents

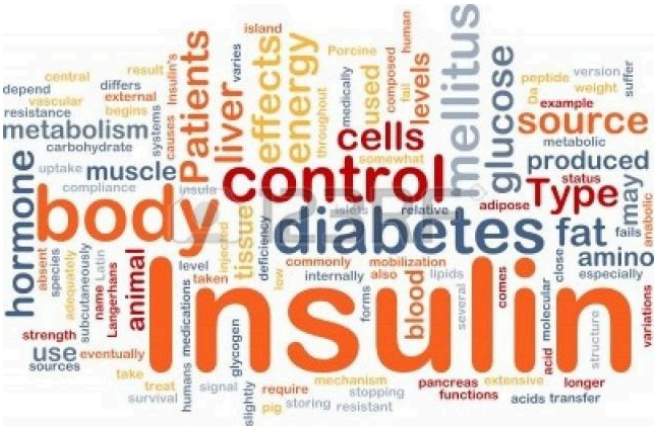
Why This Book

It's terrible news to receive. The shock when your doctor diagnoses you with diabetes or warns you that you are pre-diabetic can set you reeling. Your physician's words slam into you; the news that your lifestyle is putting your health at serious risk is a bitter pill to swallow, and a tidal wave of disbelief and fear washes over you. Your doctor notices the shock in your eyes and tries to assure you that diabetes doesn't have to dictate how your future unfolds. "Don't panic," s/he tells you, "you're not alone. 9% of the world's adult population has diabetes."[1]

Misery may love company, but when it comes to diabetes, the fact that millions of other people live with the disease does little to reassure you. All you can see is the gargantuan task of having to change, drastically, your lifestyle, monitor and control your blood sugar levels, improve your diet and begin to exercise more. And even though there are millions of others suffering from the same condition, it's up to you and you alone to take responsibility for your condition.

But don't dismiss your doctor's assurances; as a diabetic, there is nothing worse than losing a handle on your situation. Once diagnosed, there is no room for

irrational fears and reactionary behaviors. If you want to live a full, happy life, the primary rule is: take control and commit to the necessary lifestyle changes that your physician suggests. So whether you're a recently diagnosed diabetic or someone who's been battling with the disease for years, stop and take a deep breath. By choosing to read this book, you've already put yourself on an active path that can lead you towards better management of your diabetes, along with a fuller, healthier life.



If you are having doubts, consider the millions of people dealing with the same predicament, but who are leading full, happy lives. It is inspiring. Take, for example, the actor Tom Hanks, diagnosed with type 2 diabetes in 2013. "I have high blood sugars, and Type 2 diabetes, but it is not going to kill me, Hanks insisted."But I just have to eat right, and exercise, and lose weight, and watch what I eat, and I will be fine for the rest of my life."[2]

Halle Berry, who fell into a week-long coma in 2007 before being diagnosed with type 1 diabetes, described how she managed to navigate the disease and still maintain her A-list celebrity status: "I do not love to work out, but if I stick to exercising every day and put the right things in my mouth, then my diabetes just stays in check."[3]

All of her life, actress, and comedienne Sherri Shepherd struggled with emotional eating and weight gain. Diabetes was so prevalent in her family that she considered losing a limb or going blind routine. She avoided the warning signs until she was diagnosed with type 2 diabetes. That was her wake-up call. Inspired by her son to regain control of her health and life, the actress committed to improving her relationship with food. "My mom passed away at 41 from diabetes. And I'm 42, thank you. I didn't want to do that to my son. So any time I was at the gym, that thing that helped me do that last squat was my son calling some other woman, mommy. And that would just give me that extra oomph to do that last squat. I want to be around for him."

After former major league baseball player David 'Boomer' Wells was diagnosed with type 2 diabetes in 2007 he made serious changes to his lifestyle. He eliminated alcohol as well as rice, pasta, potatoes and white bread from his diet to help manage his diabetes.

Another successful athlete who dealt with diabetes throughout his career was the rugged leader of the Philadelphia Flyers' Broadstreet Bullies, Bobby Clarke. He was diagnosed at a young age with type 1 diabetes and proved skeptics, who said he wouldn't be able to play professional hockey because of his ailment, wrong.[4]

Two-time Grammy winner Patti LaBelle was diagnosed with diabetes after passing out on stage at the age 50. Determined to get her diabetes under control, the singer who claimed that was hooked on fried chicken and pasta, completely revamped how she prepared her meals.

The list of successful, healthy diabetics living full lives is long also include: Mike Huckabee, the former presidential hopeful and Fox News host who lost 105 lbs in 2003 after his doctor diagnosed him with diabetes and warned him that he wouldn't be alive in ten years if he didn't turn his life around. Larry King, who has taken diabetes medicine since 1995, advocates exercise and information. "Once you have diabetes, knowledge is a great protector. Good information is readily available. Take advantage of that. The more you know, the better off you are."

Inspiration Row

Left to right: Tom Hanks, Halle Berry, Mike Huckabee, Larry King, David Wells, Bobby Clarke, Patti LaBelle, Sherri Shepherd

Dealing with diabetes means that you'll have to do things that may seem foreign to people not suffering from the disease: like monitoring your blood glucose levels throughout the day, paying close attention to what you eat, managing your weight and planning meals. It may leave you feeling disheartened, but that doesn't mean by remaining vigilant and committed, you can't live a fulfilled and happy life.

That's why *The Ultimate Guide* is such an essential resource. The information compiled here represents the most comprehensive and cutting-edge, scientific information about diabetes. And like Larry King says, the more you know the better prepared you are to deal with your blood sugar issues.

Diabetes education is a tried and tested method to help you avoid serious complications associated with the disease. A complex ailment that requires daily self-management, most of the hard work needed to establish control over diabetes takes place outside of the physician's office. And because the responsibility to improve your health is yours alone, you need to learn new, healthier behaviors and make them part of your everyday lifestyle.

Successful diabetes control requires a positive and a willful state of mind. Unless you believe that controlling diabetes is a worthwhile endeavor, you won't be able to get a handle on it. And if you aren't committed to success, it is more than likely you'll be a slave to your diabetes instead of a master of it. It all begins with recognizing the steps that you need to take to improve your health. The simple fact is: you can't change the fact that you have diabetes, so your choice is either to deny and ignore it and risk the consequences or accept the fact that you have it and deal with it in a life-affirming kind of way.

So where do you begin? When it comes to diabetes, the long lists of potential treatments are often as obscure as they are subtle. Worse, because so many charlatans are hoping to make a buck off of your misfortune, it’s often difficult to distinguish between the snake oil and the legitimate therapies. That is why consulting a physician is such an important strategy when it comes to dealing with diabetes. But after you leave the clinic or hospital that's when *The Ultimate Guide* plays such an important role in helping you to manage your diabetes.

From the latest medical procedures to home remedies, the *The Ultimate Guide* team has thoroughly investigated all the options in order to provide you with the most up-to-date research – pros and cons – about managing your diabetes. *The Ultimate Guide* will provide you with all the hard data you need to deal effectively and confidently with your diabetes. Within the pages of this book, you will find the latest information on herbs, vitamins, minerals and probiotics and how they can improve your diabetes resiliency and better stabilize your condition. The chapter on brown fat will open your eyes about diabetes and obesity that will compel you to immediately begin implementing a strategy that will help you to increase the production of this positive, healthy fat within your body to help you to lose weight and feel more energized.

Featuring innovative nutrition facts and recipes, cutting edge exercises, and psychological tips, this resource is an invaluable aid that will help you navigate your way towards renewed blood sugar health. You'll learn about the latest scientific discoveries regarding diabetes medicines and advances in insulin that can best improve your blood sugar management with less risk of hypoglycemia. The chapter on the glycemic index will provide you with a valuable tool to determine the real sugar value contained in the foods you consume and give you an additional step up on your diabetes. Armed with this body of information you will be fully informed and motivated about all of the diabetes options available to you.

Frederick Banting (right) the first physician to treat diabetics with insulin

But remember, it's not just sound medical advice and an encyclopedic understanding of diabetes that will contribute to improving your condition. What is often at the heart of any positive change in your well-being is your desire and commitment to improving your overall health, and a willingness to make the necessary and appropriate lifestyle changes that will allow your health to improve.

So keep in mind, there will be ups and downs. There will be moments when you can better stick to your regimen. But don't be too tough on yourself or make excuses when you fall off your program. Admit that you tripped up, then try to determine why, so you can prevent another slip-up in the future.

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Diabetes Basics

Introduction

If you or someone close to you has been diagnosed with diabetes, you probably have many questions and concerns. Although it might seem like a complicated enigma, diabetes doesn't have to be a big mystery. By understanding the intricate details of diabetes, and how it affects your body, you can better position yourself to make prudent decisions about your condition, which will benefit you in the long term.

Diabetes mellitus is a metabolic condition involving problems with the hormone insulin. Insulin is released by the pancreas, which is located behind the stomach. Insulin helps the body to store and utilize the sugar and fat that comes from food. It does this by facilitating the transfer of glucose from the blood to the muscle and other tissue cells of the body.

Diabetes mellitus can be divided into three main categories: type 1, type 2, and gestational. Type 1 diabetes occurs when the pancreas produces little to no insulin. The immune system in the body of a type 1 diabetic patient attacks and destroys beta cells, which are specialized insulin-producing cells in the pancreas. Type 2 diabetes occurs when the body becomes insulin-resistant. Although the pancreas continues to produce insulin, the body cells are not able to use it effectively,

resulting in high blood sugar levels. Type 2 diabetes is generally attributed to a combination of genetic make-up, excessive body weight, and lack of exercise.

Gestational diabetes occurs among pregnant women who do not necessarily have a previous history of diabetes. During pregnancy, a woman may become insulin-resistant due to the production of hormones that can impair the activity of insulin. This disrupts normal absorption of glucose by the body's cells, causing glucose to accumulate in the blood. This leads to gestational diabetes.

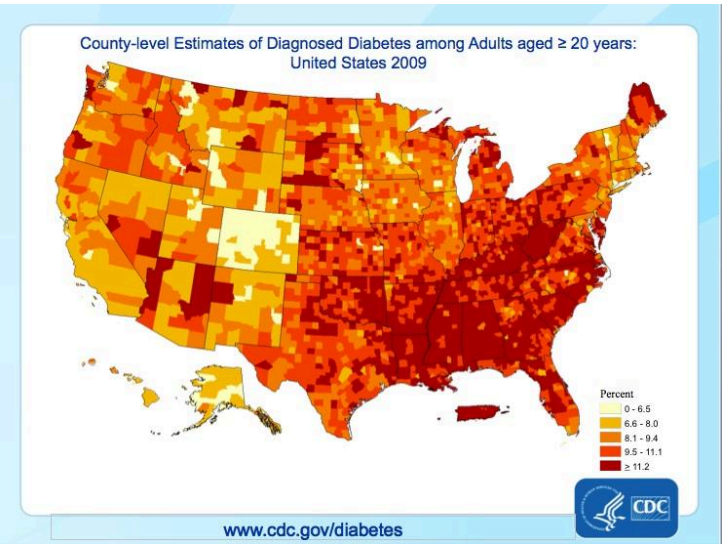
Epidemiology

This section explores the epidemiology of diabetes. Epidemiology is the study of diseases based on incidence, ethnicity, and risk factors.

On a global level, diabetes mellitus is a major cause of death and disability. In 2014, it was estimated that 8.3 percent of the world's population (close to 382 million people) suffer from diabetes. The North American and Caribbean region account for the highest incidence rate, at 11 percent (39 million people). The Middle East and Africa are next in line with a 9.7 percent incidence rate (37 million people), followed by the Western Pacific region at 8.5 percent (138 million people). [1]

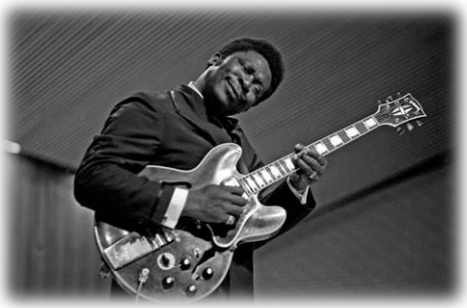
In the United States, the number of diabetes diagnoses has increased significantly over the past 20 years. The map above, based on statistics from 2009, reveals a higher prevalence in the south-eastern areas of the country. In total, over 29 million Americans have been diagnosed with diabetes, while another eight million remain

unaware of their condition. This says nothing of the 86 million Americans with prediabetes, a condition of higher-than-normal blood sugar levels that can progress to diabetes, if left unchecked.[2]



It is estimated that diabetes cost the United States $245 billion in 2012. Furthermore, diabetes was the 7th leading cause of death in the United States in 2010.[2] However, the news is not all bad. Although the prevalence of diabetes in the United States has increased over the past two decades, the number of undiagnosed diabetes cases has decreased, most likely due to improved screening and diagnosis.[3] Meanwhile, medical and technological advances have improved glycemic control amongst diagnosed diabetics. [4]

Equally crucial in the fight against diabetes is the timely diagnosis of prediabetes. As mentioned above, prediabetes is a condition characterized by high blood sugar, making one highly susceptible to developing type 2 diabetes symptoms. You may have prediabetes and be at risk of developing type 2 diabetes if you are overweight, physically inactive, or $\geq$ 45 years of age, or if you have high blood pressure, a family history of type 2 diabetes, or a previous diagnosis of gestational diabetes.



BB King, famous musician and diabetic.

Particular racial and ethnic groups in the United States are statistically more likely to develop type 2 diabetes than others. Type 2 diabetes occurs with higher frequency among African Americans, Hispanics, Native Americans, Asian Americans, and Native Hawaiians.[2]

About 19 percent (4.9 million) of African Americans over the age of 20 suffer from diabetes (undiagnosed or diagnosed), compared with 7.1 percent among non-Hispanic White Americans. This translates into African Americans being 77 percent more likely to get diabetes than non-Hispanic White Americans.[5] In 2008, African Americans were also 2.7 times more likely to start treatment for end-stage renal disease (ESRD) or kidney disease related to diabetes. They tend to be hospitalized 1.7 times more and have a 2.2 times higher mortality rate from diabetes than non-Hispanic White men.[6]

About 11.8 percent of the Hispanic/Latino American population over the age of 20 is diagnosed with diabetes.[7] The risk of diabetes among Hispanic and Latino Americans is 66 percent higher than among non-Hispanic White Americans. Latinos are also 1.6 times more likely to start ESRD-related diabetes treatment, and 1.5 times more likely to die from diabetes, than non-Hispanic White Americans.[7] Broken down by region, Latinos from Cuba and Central America, aged 20 years or older, have a 7.6 percent diabetes rate. The rate for Mexican Americans and Puerto Ricans jumps to 13.8 percent.[5]

8.4 percent of Asian Americans over the age of 20 are diagnosed with diabetes, making them 20 percent more likely to get diabetes than non-Hispanic White Americans.[5, 8]

Even more alarming is the diabetes mortality rate for Native Hawaiians: 22 percent higher than for the mainland U.S. population .[9]

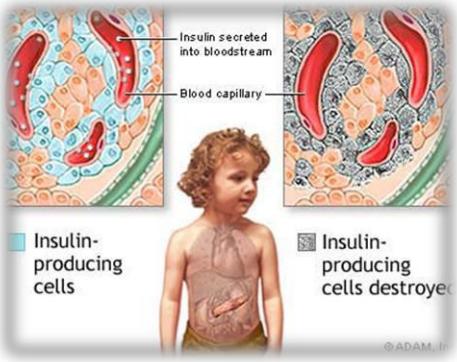
Among U.S. ethnic groups, Native Americans and Alaskan Natives have the highest age-adjusted diabetes rate, at almost 16 percent.[10] The 2008 diabetes mortality rate among Native Americans and Alaskan Natives was 1.6 times higher than the average US rate, while the rate of diabetes-related kidney failure was 1.9 times higher. [11]

The risk for type 2 diabetes increases with age. While type 2 diabetes is not considered 'curable,' it is possible to take steps to effectively manage the disease and even improve your insulin sensitivity.

Causes

The following section will provide you with important information on the biological origins of diabetes. A sound understanding of diabetes will give you a strong foundation on which to build strategies for dealing with it.

Type 1 Diabetes



The root cause of type 1 diabetes is insufficient insulin; this results from the destruction of insulin-producing beta cells located in the pancreas. Type 1 diabetes is frequently caused by an autoimmune process, in which the body's immune system mistakenly recognizes the beta cells as "foreign" elements that should be eliminated from the body. The beta cells end up being attacked and destroyed by the immune system, thus diminishing levels of insulin production.

Type 1 diabetes can manifest at any age; however, it usually develops in adolescence, before early adulthood. The incidence rate in the general population is about 1 in 300.[12]

Environmental Factors

Cold weather and exposure to toxins have both been reported to trigger type 1 diabetes.[13] It has also been speculated that fastidious hygiene practices and clean environments have reduced exposure to germs that bolster the immune system.

These heightened sanitation levels might predispose individuals to dysfunctional immune responses associated with increased incidences of allergies, asthma, and type 1 diabetes.[14]

Prenatal influences

There are several indications that the period spent in the womb may influence a child's subsequent risk of diabetes. One theory posits that you are more likely to develop the condition if your mother is affected instead of your father. Also, the risk of getting type 1 diabetes is slightly increased by higher birth weight.[13]

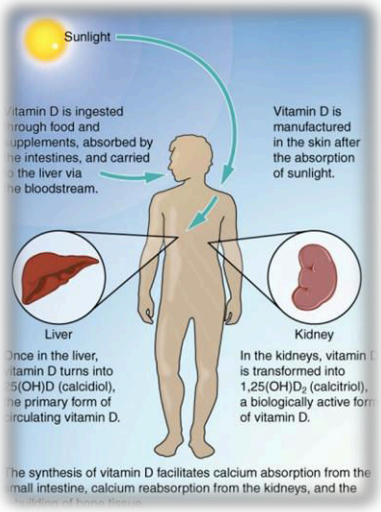
Viruses

Viruses penetrate cells and reconfigure the way they are recognized by the immune system. Scientists have described numerous ways by which viruses can compromise beta cells. Although a virus on its own cannot cause diabetes, some people are diagnosed with type 1 diabetes during a viral infection or after recovery. Thus, autoimmune responses against the pancreatic beta cells might be triggered by viral infections; however, the evidence remains circumstantial.[15]

Milk and Cereal Proteins

Studies have noted that dietary factors may increase or reduce the risk of type 1 diabetes. For example, infants who are breastfed may be less likely to develop the condition, while infants exposed early to cow's milk and cereal proteins may have an increased risk. However, further research is required to confirm these connections.[15]

Vitamin D



Vitamin D is obtained from food and is also generated in the skin in response to sunlight. Many researchers believe that vitamin D helps to boost the efficiency of immune cells, by enhancing their function and facilitating their communication with one another. In the context of type 1 diabetes, vitamin D may help to prevent immune cells from destroying beta cells in the pancreas.[16]

Vaccination

Parents can be assured that despite rumors and speculation, there is little to no scientific evidence indicating that routine vaccinations can induce the risk of childhood diabetes.[17]

Type 2 Diabetes

Type 2 diabetes is the most common form of diabetes and is caused by a number of factors. Insulin resistance results when the body's muscle, fat, and liver cells fail to use insulin effectively. Insufficient insulin production in the body, along with impaired sensitivity to insulin, results in the development of type 2 diabetes. Sometimes symptoms may develop slowly, so that some people with type 2 diabetes remain undiagnosed for years.[15]

Middle-aged and elderly people who are overweight are the most prone to developing type 2 diabetes. However, this disorder is also being seen increasingly among overweight or obese children and adolescents.

Genetic Susceptibility

The link between type 2 diabetes and family history is stronger than with type 1. Among twins, for example, the risk is as high as 3 in 4 if your twin has type 2 diabetes.[13] However, you are not guaranteed to develop the disease if one, or even both, your parents suffer from it.

There are several genes that have been implicated in the heritability of type 2 diabetes, including *TCF7L2* variants. For people who inherit two copies of these variants, the chance of developing type 2 diabetes is about 80 percent higher than for individuals without these variants.[15]

Even if there is a family history of your diabetes condition, it is to distinguish whether lifestyle or genetics is the primary causative factor. In all likelihood, both have a role to play. Yet despite the probable genetic component, research has indicated that exercising and losing weight can delay, prevent, and even reverse type 2 diabetes.[18]

Obesity and Physical Inactivity

Physical inactivity and obesity are strongly associated with insulin resistance and type 2 diabetes. Central obesity (the accumulation of excess abdominal fat) is a serious risk factor

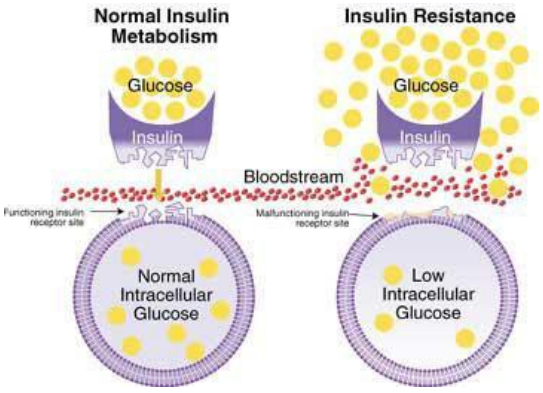
not only for insulin resistance but also for cardiovascular disease. Excess "belly fat" produces hormones and other substances, which can cause harmful long-term damage to blood vessels.[15]

Insulin Resistance

If you have insulin resistance, do you necessarily have type 2 diabetes?

If your doctor has told you that you're insulin resistant, you're probably asking yourself this very question. Fortunately, the answer is "no." Not everyone with insulin resistance is diabetic. With insulin resistance, your body can't respond properly to the insulin it produces, raising your blood sugar levels. Increased blood sugar can lead to heart disease and type 2 diabetes. However, heart disease and type 2 diabetes are not inevitable. A good diet and regular exercise can prevent the onset of heart disease and type 2 diabetes, and prolong your life.[15]

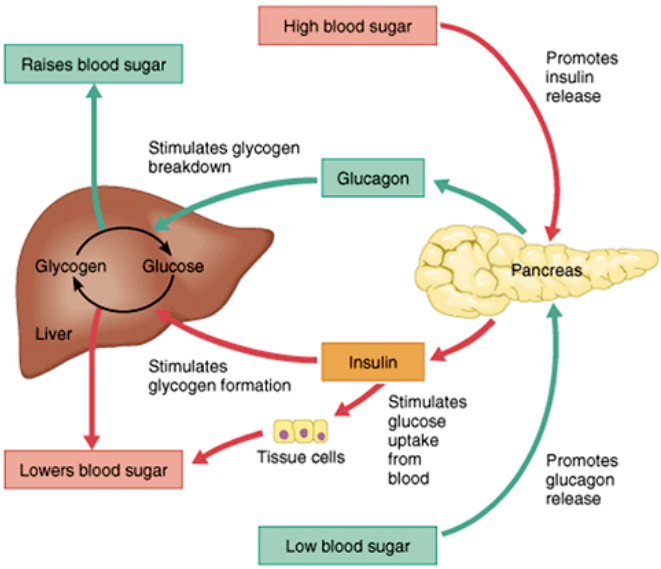
Metabolic Syndrome



Metabolic syndrome (also known as insulin-resistance syndrome) is characterized by several conditions common among people with insulin resistance. These include:

- Above-normal blood glucose levels
- A larger waist size due to excess abdominal fat
- High blood pressure
- Increased concentration of cholesterol and triglycerides in the blood

Individuals diagnosed with metabolic syndrome have a higher risk of developing type 2 diabetes and cardiovascular disease. Research has found that lifestyle changes, such as exercise and shedding excess pounds, are the most effective means of reversing metabolic syndrome, improving insulin response, and reducing the risk of type 2 diabetes and cardiovascular disease .[15]



Abnormal Glucose Production by the Liver

In some cases, abnormal glucose production by the liver contributes to high blood glucose levels. This is caused by excess levels of the hormone *glucagon.* Glucagon signals the liver to release stored glucose into the bloodstream, and is normally released by the pancreas when blood glucose and insulin levels are low. After eating, your blood glucose and insulin levels are elevated and glucagon levels are reduced, allowing excess glucose to be stored by the liver for future use. However, in many people with diabetes, glucagon levels may remain high after eating, causing the liver to release unneeded glucose and raising blood glucose levels. The drug Metformin is commonly taken by type 2 diabetics to reduce this excess glucose production by the liver.[15]

Cell Signaling and Regulation

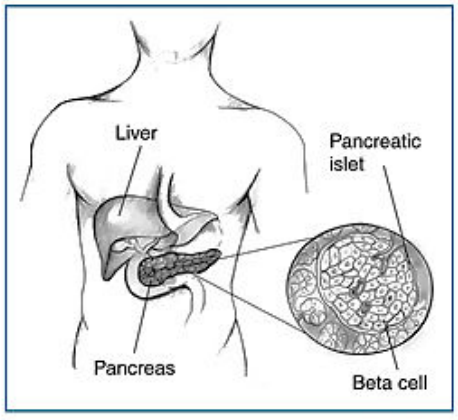
Problems in cell signaling affect the ways cells communicate with each other, potentially leading to disease. Studies of diabetes are focused on insulin signaling pathways, helping us to understand insulin resistance and the dysregulation of glucose uptake.

Several different causes of insulin resistance have been proposed. One theory holds that it is triggered by important inflammatory substances released from fat cells. Another contends that insulin resistance results from a disruption to the insulin pathway. Glucose uptake dysregulation results from problems in the insulin signaling pathway. Normally, insulin binds to insulin receptors in body cells, enabling these cells to take up glucose from the blood and convert it into energy. Disruption of this process (e.g. through reduced insulin release or insulin resistance) can inhibit glucose uptake by the body's cells, leading to increased blood glucose.

More research into these cell signaling pathways may further the development of new treatments for diabetes.[15]

Beta Cell Dysfunction

Abnormalities in the function of beta cells contribute substantially to the development of type 2 diabetes. Malnutrition occurring early in life may be one cause of this beta cell



dysfunction. Beta cell defects can lower insulin release, which can lead to glucose toxicity, followed by further beta cell damage.[15] These defects in beta-cell function have been studied using isolated islet cells taken from pancreatic tissue.[19]

Gestational Diabetes

Several factors are believed to contribute to gestational diabetes, including genetics, environmental factors, hormonal changes, and increased metabolic stresses from pregnancy.[15] Estrogen, progesterone, and human placental lactogen (HPL) are some of the hormones produced during pregnancy; these cause cells to lose their sensitivity to insulin, leading to high blood glucose levels .[20]

Although these hormones provide extra glucose and nutrients in the blood for fetal development, they may also cause the mother's body to become insulin resistant. This can happen because some pregnant women are unable to produce sufficient amounts of insulin to deal with the high blood glucose levels, and/or their body cells no longer respond effectively to insulin.[20]

Here are the characteristics that can increase your risk of gestational diabetes[20, 21]:

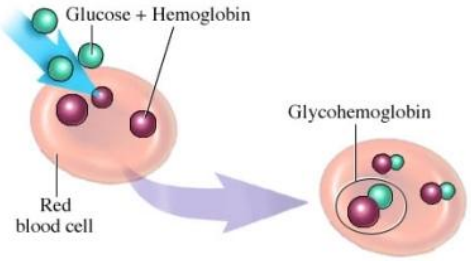
- Your body mass index (BMI) is 30 or higher.
- You have previously delivered a baby who weighed over 9 pounds.
- You had gestational diabetes during a previous pregnancy.
- You have a history of diabetes in the family.

- Your ethnicity is African American, South Asian (India, Pakistan), Asian, Hispanic, or American Indian.

Diagnosis and Screening

High blood sugar levels can negatively affect your health before you begin to notice diabetes symptoms. Thus, diabetes tests that measure blood sugar are crucial to helping you catch diabetes early. We recommend getting an annual diabetes test, including a blood test called the hemoglobin A1C (HbA1C) test. Other diabetes tests include the dilated eye exam and foot exam.

Importance of Hemoglobin A1c Test



The hemoglobin A1C (HbA1C) test measures a person's average blood glucose levels over a three-month period. Hemoglobin is a component of your blood cells that helps to transport oxygen throughout your body. If there is a sharp increase in your blood sugar, sugar molecules start attaching to the hemoglobin, which is then said to be "glycated." The greater the level of glycated haemoglobin in the blood, the higher the HbA1C reading.[22] Also known as the A1C test or the glycohemoglobin test, HbA1C is the foremost test for diabetes management and research.[23]

The normal HbA1C level is usually around 5 percent in non-diabetics. However, a person suffering from uncontrolled diabetes may have an HbA1C level above 7

percent.[22] A diagnosis of diabetes is given if your HbA1C level is 6.5 percent or higher on two separate tests. Prediabetes falls between 5.7 and 6.4 percent and indicates a high risk of developing diabetes.[24]

The HbA1C test is an indicator of how well your diabetes is being controlled over a 2- to 3-month period. When used alongside home blood sugar monitoring, the HbA1C test can help you make the necessary adjustments to your diabetes medications.

A Dilated Eye Exam

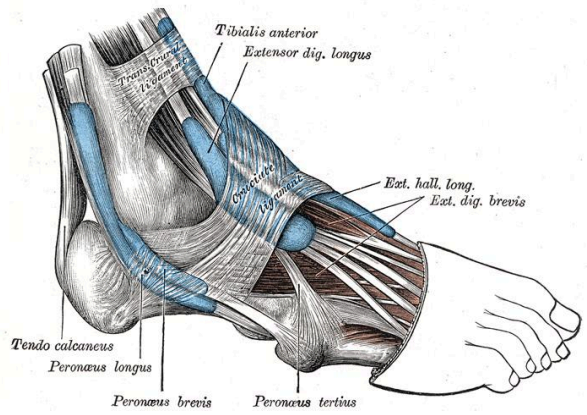
Diabetic eye diseases are a group of vision problems faced by diabetics. They can cause severe vision loss and even blindness.

By using eyedrops to widen (dilate) your pupils, it becomes easier for your physician to examine the back of your eye for signs of diabetic eye disease. Signs of disease include changes to or leaking of blood vessels, retinal swelling, fatty deposits on the retina, and damaged nerve tissue.[25]

It is important for diabetic individuals to have dilated eye exams at regular intervals. The longer you've been suffering from diabetes, the higher the likelihood that you might develop eye problems. Keep in mind that by the time you start noticing vision problems, your eyes may already be seriously damaged. Therefore, it is imperative that you schedule regular, comprehensive eye exams to catch problems before they become too severe.[25]

Foot Exam

After a long day of standing at work, it's normal to experience some foot discomfort. However, severe foot pain that seems out of proportion to your physical activity may be a telling sign of diabetes. What starts out as a minor foot problem could indicate a more serious medical condition.



This is why a comprehensive annual foot exam is so important. One in four people with diabetes will develop foot problems that require treatment. Diabetes can cause the nerves in your feet to become damaged, thus reducing your ability to detect pain and discomfort.[26]

A foot exam involves a visual inspection of your feet to check for skin discoloration, or other signs of damage, such as cuts and bruises. Your doctor will also carry out sensation tests with a tuning fork, or a tool called a monofilament, to check for numbness.[27]

Diabetes Symptoms

Increased thirst, hunger, and urination frequency are all symptoms of high blood sugar. When left unchecked, diabetes can cause countless complications. Acute complications include diabetic ketoacidosis, a life-threatening condition caused by insufficient insulin, which can eventually lead to coma. Serious, long-term

complications can include cardiovascular disease, stroke, chronic kidney failure, foot ulcers, and damage to the eyes.

Type 1 diabetes and type 2 diabetes are both chronic conditions. However, prediabetes can be reversed; with this condition, blood sugar levels are higher than normal, but not high enough to be classified as diabetes. Gestational diabetes is another reversible condition. It occurs during pregnancy, but may resolve after the baby is delivered.

Initial symptoms of diabetes, especially type 2 diabetes, can be subtle and seemingly harmless. But take heed: in the United States alone, more than 8 million people have undiagnosed diabetes, according to the American Diabetes Association.[28] By speaking to your physician about potential diabetes symptoms, you can get an early diagnosis and treatment, and a lifetime of better health. What follows is a description of different diabetes signs and symptoms. If you're experiencing any of these, be proactive: make an appointment to see your doctor *immediately.*

Excessive Thirst and Increased Urination

One of the earliest diabetes symptoms is heightened thirst. This is usually accompanied by excessive dryness of the mouth, and increased blood sugar levels. You'll feel the need to urinate more frequently, because your body has to expel excess sugar through the urine. This causes more fluids to be drawn from your body, leaving you dehydrated and thirst.[29, 30]

Fatigue

Many people with diabetes complain that they often feel tired and lethargic. Many factors can contribute to this, including sugar levels that are either too high or too low. In both cases, fatigue is caused by ineffective or insufficient amounts of insulin, which provides the body's tissue cells with sugar.[31]

Weight Loss

Weight fluctuations are also potential signs of diabetes. Frequent urination leads to calorie loss. At the same time, you may feel ongoing hunger, since diabetes prevents sugar from reaching your cells. This one-two punch can lead to rapid weight loss, common among type 1 diabetics.[30]

Blurred Vision

Maybe you don't need new prescription lenses after all – maybe that blurred vision you are experiencing is actually being caused by high blood sugar levels. The eye swells when blood sugar levels get too high, inhibiting your ability to see clearly. If left unchecked, new blood vessels may form in the retina, causing damage to existing

vessels. When caught early, these changes normally do not cause vision problems. However, without treatment, they can eventually lead to vision loss and blindness.[30]

Slow-Healing Sores or Frequent Infections

Wound healing can take longer when the patient is diabetic. High blood sugar can affect blood circulation and cause nerve damage, which may impair your body's healing process. And a slow-healing wound can worsen rapidly, so it is essential for diabetics to monitor their wounds carefully.[29, 30]

Tingling or Numbness in Hands and Feet

Pain, tingling, or numbness is a sign of nerve damage, which is commonly associated with diabetes. Over time, excess levels of blood glucose can damage peripheral nerves, leading to diabetic peripheral neuropathy. Although diabetic peripheral neuropathy can affect any part of the body, the most frequent symptoms are abnormal sensations in the toes and feet. These sensations generally include sharp or shooting pains, burning sensations, tingling, and a feeling of being pricked with pins. Numbness and tingling can also be experienced in the hands and arms.[32]

Gum Disease

Diabetes can undermine your mouth's germ-fighting ability, increasing your chance of oral infection and gum disease. High blood sugar levels can worsen gum disease, and gum disease can in turn contribute to high blood sugar, making diabetes harder to control.

You may have gum disease if your gums bleed, or if they feel irritated, swollen, and tender. Your gums may also start to detach from your teeth, exposing the root of the tooth, or forming pockets that fill with germs and pus. If left untreated, gum infections can end up destroying the bone around your teeth, causing your teeth to loosen or fall out.[33]

Gum disease often doesn't cause any physical discomfort. This means that you may remain unaware of the condition until you have some serious damage. Regular visits to the dentist are therefore your best weapon.

Acetone Breath

This may sound far-fetched, but your breath can help to determine how well you are maintaining your blood sugar levels.[34]

If your diabetes isn't being controlled properly, then insufficient levels of glucose are being taken up by your body's cells. Without enough glucose, your body will begin burning fat for energy. This will cause ketones and waste products to

accumulate in the blood, and subsequently the urine. Acetone is one type of ketone; it can be detected in your breath due to its fruity smell.[35]

High ketone levels indicate that you are not properly managing your diabetes. If left untreated, ketone buildup can develop into diabetic ketoacidosis, a dangerous condition that can lead to coma. A vigilant diabetes care plan should include guidelines for monitoring your ketones, either involving blood tests or a urine test.[36]

Pay more attention to your body's hints

Consult your doctor if you notice anyof the above warning signs of diabetes. This will help to diagnose your condition early, enabling proactive treatment. Diabetes is certainly a serious disorder; however, your vigilance for signs and symptoms, and the dependable support of your health care provider, can make all the difference.

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Complications Associated with Diabetes

Introduction

Diabetes increases your chances of developing a number of health problems. That's why it is important to stay vigilant against skin infections, eye complications, and neuropathy. You also need to embrace an effective diabetes treatment plan, including positive lifestyle changes to prevent or delay the onset of the complications associated with your disease.

Now let's preface this chapter with an explanation. The information covered in this section is very scientific and technical. Of course, it may not be the most engaging material you've ever read, but unlike a novel at the top of the best-seller list, the information here is not fiction. On the contrary, what you'll learn here are the hard facts about diabetes complications – hard facts that could save your life.

During a 2005 Banting lecture, diabetes pioneer and visionary Michael Brownlee discussed the perils of type 1 and type 2 diabetes. Being a type 1 diabetes survivor himself, he is intimately aware of the complications arising from diabetes.

Brownlee noted that the discovery of insulin gave a lot of hope to diabetics. However, insulin therapy alone was unable to treat many of the complications of diabetes. These complications include kidney problems (nephropathy), cardiovascular disease, eye complications (retinopathy), and ulcerations due to nerve damage (neuropathy).[1]

Today, there are treatments that can delay the onset of these complications in diabetics and, in people already affected, delay their progression. Research continues to focus on improving existing therapies and on observing the potential benefits of combination therapies.

Diabetes is not an isolated condition, but is associated with other complications, some of which affect the blood vessels. Microvascular complications (affecting the capillaries) or macrovascular complications (affecting the veins and arteries) can often be observed in diabetic individuals. Such changes are caused by hyperglycemia,[2,3] and can be observed in the eyes, retinal cells, kidney renal cells, and the nerve cells. These specific cells are unable to control glucose concentrations in the presence of hyperglycemia.[1] Specific molecular changes occur in these cells, which render them inefficient at regulating internal glucose concentration. In this chapter, we will avoid many of the technical details of these molecular changes, but we will offer a brief outline.

Hyperglycemia induces the production of a large number of reactive oxygen species (ROS), which are chemically reactive molecules containing oxygen. These molecules cause DNA damage to retinal cells, renal cells, nerve cells, and cardiac cells.[1] This damage can give rise to both microvascular and macrovascular complications, exhausting in the process all of the important antioxidant molecules that wage war against ROS.

Antioxidants are your body's cavalry, helping to maintain balance in your body by absorbing oxidizing molecules. In the absence of these antioxidants, ROS can damage your nerves and contribute to diabetic microvascular and macrovascular complications.[2]

Another observed molecular change in the cells of diabetics is an increase in the production of advanced glycation end products (AGE). These products modify the internal and the external environment of the cell, resulting in inflammation and plaque build-ups, which narrow the blood walls of the heart.[1, 4]

Ultimately, blood vessel complications caused by diabetes can give rise to other disabling conditions. Diabetic nephropathy associated with kidney damage, neuropathy, and retinopathy are all connected to microvascular complications in diabetic patients.[2,3,5] Macrovascular complications include stroke, heart disease, and peripheral arterial disease.[2,3,6] Other effects of microvascular and macrovascular complications can include erectile dysfunction and cancer, while age, puberty, and prolonged diabetes are some of the risk factors contributing to these complications.[6-8]

Microvascular complications

Diabetic Nephropathy

Diabetic nephropathy is a disease caused by damage to the *glomeruli* of the kidneys (one of the kidneys' filtration apparatus), and it is observed most frequently in Native Americans, Asians, and African Americans. This condition results from a dysfunction in the protein albumin. Normally, albumin binds to the blood and helps to maintain fluid balance. However, in the nascent stage of diabetic kidney disease, the kidneys start expelling too much albumin from the blood through urination. This disorder is known as microalbuminuria. In a normal

person, less than 25 milligrams of albumin is excreted in the urine each day. However, in a person with microalbuminuria, the concentration of albumin in the urine is between 30 and 300 milligrams per liter. Microalbuminuria is not uncommon in people who have had diabetes for five or more years.[2,9,10]

Risk Factors

So how, you might wonder, does diabetic nephropathy develop? Diabetic patients develop Microalbuminuria when high blood pressure and high levels of blood glucose remain unchecked. One third of people suffering from diabetes for more than 15 years develop diabetic nephropathy.[3]

Genetic predisposition, puberty, and elevated blood pressure can all potentiate diabetic nephropathy in patients with type 1 diabetes. In the 1980s, nearly 80% of type 1 diabetes patients with microalbuminuria developed macroalbuminuria (greater than 300 milligrams per liter). However, thanks to appropriate glycemic control measures and blood pressure control, the number of diabetics with microalbuminuria who develop macroalbuminuria has been reduced by nearly half.[10]

Another essential part of effective microalbuminuria management is early diagnosis. Following diabetes diagnosis, it is necessary that the patient be screened for microalbuminuria. Type 2 patients should be screened as soon as they are diagnosed with diabetes, while for type 1 patients, screening is recommended five years after their initial diagnosis. However, if type 1 patients follow a poor diet regimen or have just reached puberty, it is recommended that they be screened for

microalbuminuria one year following diagnosis. Even in the absence of microalbuminuria, it is required that type 1 and type 2 patients be screened every year for diabetic nephropathy.[10]

Interestingly, there are some cases where urinary albumin excretion (UAE) levels have been seen to return to normal (normoalbuminuria).[10]

Diagnosis

The standard diagnostic procedure for diabetic nephropathy involves measuring the albumin content of the urine. This procedure is referred to as a *spot urine sample*. If the doctor suspects microalbuminuria, the diagnostic procedure needs to be confirmed two additional times within 3 to 6 months. A cut-off UAE value of 17 mg per liter confirms the presence of microalbuminuria.

Even in diabetic patients with normal UAE, it is possible to have a decrease in the glomerular filtration rate (GFR) of the kidneys, leading to further protein loss. Therefore, GFR needs to be measured alongside UAE to determine the presence of diabetic nephropathy.[2,10]

Keep in mind that type 2 diabetes patients show greater structural changes in the kidneys than type 1 diabetic patients.[10]

A *renal biopsy*, where a small piece of the kidney is removed for medical examination, is recommended for patients who display proteinuria (excess protein in the urine), diabetes, and a decline in kidney function. Also keep in mind that

diabetic nephropathy is a predisposing condition for heart disease, and that if you are diagnosed with diabetic nephropathy, your heart should be routinely evaluated using medical imaging technologies.[10]

Treatment

There are many treatment interventions for diabetic nephropathy, depending on the symptoms and the diagnosis.[10]

Treatments for anemia

Anemia occurs when there is a lack of red blood cells or hemoglobin in your body. This condition is often observed in patients with diabetic nephropathy. It is recommended that individuals suffering from anemia be treated with erythropoietin, a hormone that stimulates red blood cell production.[10]

Diet

If you are dealing with diabetic nephropathy, doctors recommend replacing red meat with white meat (chicken or turkey), as a restricted protein intake can limit the progression of diabetic nephropathy.[10]

Relieving blood pressure

Diabetic nephropathy is associated with hypertension. However, the progression towards diabetic nephropathy from hypertension can be combated with ACE (angiotensin converting enzyme) inhibitors, ARBs (angiotensin II receptor blockers), or a combination of the two.[2]

Statin medications and aspirin are also used to treat cardiovascular conditions associated with nephropathy.[10]

Diabetic Eye Conditions

Diabetes can trigger eye diseases like glaucoma, cataract, and diabetic retinopathy. Diabetic retinopathy occurs when the blood vessels in your retina are damaged, and it is the primary cause of blindness in the United States. In certain cases of retinopathy, new blood vessels are formed abnormally, while in others, blood vessels start to leak fluid after swelling up.[11]

In type 2 diabetics, the development of diabetic retinopathy is dependent on the severity of the hyperglycemia and hypertension, and on the length of time that they have been present. It may even begin to develop prior to a type 2 diabetes diagnosis. In general, type 1 diabetic patients develop diabetic retinopathy within a period of 20 years of diagnosis. It poses a serious risk for diabetic women who are pregnant; these individuals will require regular follow-up eye exams to detect the condition.[2,11]

There are two classifications of diabetic retinopathy: proliferative and background.[2] Proliferative diabetic retinopathy results from the emergence of new blood vessels in the retina and from spots that form on the retina.Take heed; if left untreated, this retinopathy can lead to permanent blindness.[2] The good news is that laser correction interventions can slow the progression of this condition.

Background diabetic retinopathy results from hemorrhagic spots (dots) developing on the retina. Lipid deposits and blood vessel dilatations appear, along with these

red spots. In the absence of appropriate treatment, vision loss may result.[2] Unfortunately, diabetic retinopathy often occurs together with diabetic nephropathy. Patients with one tend to suffer from the other to varying degrees.[10]

Risk factors

Factors such as growth hormones and vascular endothelial growth factor (VEGF) contribute to the development of diabetic retinopathy. Diabetic retinopathy can develop as follows: hyperglycemia causes elevated levels of glycoproteins. This increase in blood glucose results in an accumulation of sugars in the cells, which can then cause diabetic eye complications. These high glucose levels also cause a dangerous increase in reactive oxygen species.[1,2,9]

Symptoms

Macular edema occurs when there is a leakage of fluid into the macula (central region of the retina), leading to blurred vision. Abnormal blood vessels that arise in the retina can also result in diminished vision.[11]

Diagnosis

Eye dilation: Drops are added to the eye to dilate the pupils. This permits a better view of the eye, making it easier for your physician to detect abnormal blood vessels and other problems with the retina. Visual acuity is a standard vision test. The assessor uses a chart to test how well the eyes see at varying distances. Tonometry measures the pressure within the eyes.[11]

Treatment

Major things to consider when addressing diabetic retinopathy are the importance of controlling blood pressure, blood cholesterol, and blood glucose levels.

Vitrectomy is a procedure designed to remove excess blood from the center of the eye. An incision is made in the eye and the excess blood is replaced with a saline solution. Medications are required to prevent infection. If you do opt for this procedure, an eye patch must be worn for several weeks following surgery, in order to protect the eye.[11]

Scatter laser treatment is used to treat proliferative diabetic retinopathy. It involves the use of lasers to shrink blood vessels in an area of the retina, and it requires multiple sessions. Consult your physician before considering scatter laser treatment.[11]

Macular edema is treated by focal laser treatment, which is similar to scatter laser treatment. This procedure results in few laser burns and requires just one session to help control the fluid leaking into the retina. Certain drugs have been developed that may be used in conjunction with lasers to treat diabetic retinopathy. These drugs have even shown promise in the absence of lasers.[11]

Laser treatment is generally performed in a physician's office, and the eyes are numbed with eye drops during the procedure.[11]

Diabetic Neuropathy

Diabetic neuropathy is nerve damage that may occur in any part of your body, including the heart and the digestive tract. It is especially common among diabetics who have suffered from the condition for more than 25 years, and it affects between 60% to 70% of diabetics.

The symptoms of diabetic neuropathy can either be painful or painless.[12] Since progressive ulceration can occur without pain, a physical examination is especially important to ensure early detection.[2]

There are 7 distinct types of diabetic neuropathy:

Focal neuropathy

This form of neuropathy affects specific nerves in the feet, eyes, ears, legs, facial muscles, chest, thighs, lower back, and pelvis.[13]

Autonomic neuropathy

This affects nerves in the urinary system, heart, digestive tract, lungs, eyes, sweat glands, and sex organs. It is associated with significant morbidity and mortality.[2,13]

Peripheral neuropathy

With this condition, the nerves in the arms, hands, feet, legs, and toes are affected. This can lead to ulcers in the feet, which may eventually require amputation.[13] Research by Frederico G Hawkins has shown that there is an intricate connection between peripheral neuropathy and macrovascular complications. Peripheral neuropathy appears to be a risk factor for stroke, cardiovascular complications, and

peripheral vascular disease. The authors recommended early screening for macrovascular complications in individuals diagnosed with peripheral neuropathy.[17]

Chronic sensorimotor distal symmetric polyneuropathy

This common form of neuropathy results in a tingling sensation and numbness in the nerve endings. Pain is often experienced, together with a loss of sensation. This condition frequently results in foot ulcers or the loss of reflexes in the ankle.[2]

Sensory neuropathy

This form of neuropathy is rare and occurs when there is poor management of the glycemic index. The symptoms, which include pain, are observed at night.[2]

Proximal neuropathy

This condition affects the nerves of your legs, buttocks, thighs, and hips. If you're suffering from this condition, you will often require assistance when standing or sitting down.[13]

Mononeuropathy

This form of neuropathy may affect any of your nerves and may occur suddenly, without warning. Mononeuropathy is characterized by both muscle weakness and pain.[2]

Risk Factors

There are numerous ways of developing diabetic neuropathy. Primary causes includea high blood sugar count, low levels of insulin, and high levels of blood fat.

Smoking and alcohol consumption also contribute to nerve damage, along with genetics.

Diagnosis

Diabetic neuropathy can be diagnosed in the following ways[13]:

Variability in heart rate

Your heart is checked for its response to different postures, variations in breathing, or changes in blood pressure.

Electromyography or conduction through damaged nerves

This procedure assesses damage to your nerves by measuring the response of the muscles to electrical stimulation of adjacent nerves.

Ultrasound

This imaging technique is used to observe the effects of diabetic neuropathy on your internal organs.

Examination of the foot

Since one of the major symptoms of diabetic neuropathy is ulceration of the foot, foot exams should be carried out regularly. In a footexam, your doctor examines your feet thoroughly, including the muscle, skin, bone, sensation, and circulation. Your foot sensations are checked with a nylon filament. Finally, a tuning fork helps to assess how well your foot perceives subtle vibrations.

Symptoms

The symptoms of diabetic neuropathy include numbness, pain, and a tingling sensation.[13] The pain can range from a shooting feeling to a burning or aching sensation.[12] Muscle wasting in the hands or feet, urination issues, feelings of weakness and/or dizziness when sitting or standing, constipation, nausea, vomiting, indigestion, dryness in the vagina, and erectile dysfunction are some of the other symptoms of diabetic neuropathy.[13]

Treatment

Diabetic neuropathy does not have any one specific treatment. Some of the currently implemented treatments are discussed below[12]:

Controlling blood glucose levels

This is one of the primary objectives when halting the development of diabetic neuropathy.

Drug therapy

This form of therapy has not been found to be extremely effective, and the drugs involved can also have side effects, such as sweating, constipation, dryness of the mouth, blurring of vision, and sedation. Drugs commonly used include capsaicin, tramadol, and oxycodone.[12] The drug duloxetine has been found to be effective at treating painful diabetic neuropathy. Erectile dysfunction, vaginal dryness, and urinary tract infections may also be treated with the appropriate medications.[13]

Alternative treatments

Small research studies have observed beneficial effects of percutaneous electrical treatment, electromagnetic stimulation of the nerves, and acupuncture on painful diabetic neuropathy.

When it comes to treating painful diabetic neuropathy, you need to understand the cause of the pain. Therefore, a multi-pronged therapy, incorporating medication and psychological analysis, may be effective at treating painful diabetic neuropathy. A multi-faceted treatment plan is also the most effective way to manage painful diabetic retinopathy.[12]

Having elaborated on the characteristics of microvascular complications, let us now focus on the different macrovascular issues associated with diabetes.

Macrovascular complications

Type 2 diabetes is a major risk factor for such conditions as stroke and heart disease. The major cause of these macrovascular complications is the narrowing of the arterial walls throughout your body. This arterial narrowing is called *atherosclerosis*. Diabetic complications may also derive from increased concentrations of blood lipids, cardiovascular conditions, high blood pressure, and an increase in blood clotting factors. All of these conditions contribute to cardiovascular disease, which is a major cause of mortality among type 1 and type 2 diabetics.[2]

Cardiovascular Disease

Among individuals with cardiovascular disease, the mortality rates of diabetics are higher than those of non-diabetic individuals. The high blood pressure and/or hypertension among type 2 diabetics contribute to their higher mortality rates.[7,14] Besides hypertension, type 2 diabetics also display increased coagulability (clotting), obesity, and hyperlipidemia (increased lipid levels), all of which raise the risk of cardiovascular disease.[2] In type 1 diabetics, cardiovascular disease is linked to defective kidney function.[14]

Type 2 diabetes heightens the risk of heart disease in women. Similarly, women over the age of 40 with type 1 diabetes show a greater risk of heart disease.[2]

Cholesterol can cause atherosclerosis in diabetics. Lowering lipid concentrations by increasing high-density lipoprotein (HDL) – good cholesterol – and lowering triglyceride concentrations are both effective means of reducing the risk of cardiovascular disease in diabetics. Fibric acid derivatives and statins (pravastatin, lovastatin, simvastatin) are also effective at lowering lipid concentrations.[2] However, a recent animal study observed that statins may have an inhibitory effect on insulin production, and may thus inhibit glucose metabolism. Therefore, statins may have a detrimental effect on diabetes.[6]

Changes in lipid concentrations are associated with obesity in type 1 and type 2 diabetics.[7]

Lowering blood pressure or hypertension is an effective means of reducing cardiovascular disease and macrovascular complications associated with diabetes.

Blood pressure can be lowered in type 2 diabetics by multi-drug therapy, specifically inhibitors of the 52 signal-angiotensin pathway.[2]

Glycemic control

Glycemic control is effective at controlling macrovascular diseases associated with diabetes.[2] One comprehensive study has demonstrated that improved glycemic control reduces macrovascular complications in type 1 and type 2 diabetes patients.[15]

Sleep Apnea

Evidence suggests that obstructive sleep apnea is a very common problem among type 1 diabetics. Individuals affected by sleep apnea often have other macrovascular complications, such as hypertension and cardiovascular conditions.[16]

Foot Ulcers

Ulceration of the foot, known as diabetic foot, is another macrovascular complication connected with diabetes. Loss of feeling in the foot, due to high blood sugar, can result in nerve damage. Ulcers develop in the foot as a result of cuts and other injuries, sometimes making amputation necessary.[18] A novel therapeutic strategy employs topical autologous platelet-rich gel, which contains blood plasma and medicine to promote healing.[6,19]

Cancer

Although the exact mechanism is unknown, it has been observed that diabetes can contribute to the rise of certain cancer types, such as pancreatic and breast cancer.[21-23] Conditions associated with diabetes, such as obesity and hyperglycemia, may also induce cancer. However, in some cases, diabetes can actually reduce the risk of cancer, as in the case of prostate cancer.[20]

In turn, individuals with cancer can be at an increased risk for diabetes. Specifically, pancreatic cancer has been noted to contribute to type 1, type 2, and type 3c diabetes.[24]

Present and Future Therapeutic Strategies for Diabetic Complications

Microvascular and macrovascular complications occur via complex signaling pathways. Understanding these pathways can help you decipher the appropriate form of treatment required. Based on the current data, reductions in hypertension, hyperlipidemia, obesity, and hyperglycemia are crucial to limiting the impact of diabetic complications. It is also important to arrange for a screening of the kidneys to better identify diabetic complications.[14]

Glycemic control is an effective way to manage both the production of advanced glycation end products (AGEs) and the onset of microvascular complications. However, there is no evidence at present to suggest that glycemic control is effective at treating macrovascular complications.[4,25]

Free oxygen radicals contribute substantially to diabetic complications. Nonetheless, unique treatment approaches are becoming available that target the production of free radicals in cells. These approaches are still in the research phase, yet they show promise as effective treatment strategies for microvascular and macrovascular complications. One of the molecules generated by free oxygen radicals is called PARP (Poly-ADP Ribose Polymerase). Inhibitors of PARP have been shown to be effective at inhibiting the effects of free oxygen radicals, as well as the production of such harmful molecules as AGEs, N-acetyl glucosamine, and protein kinase C. These inhibitors are still under study, but they have shown promise in the treatment of retinopathy.[1]

Another therapeutic approach looks at treating cells with molecules that mimic the antioxidant enzyme or protein called superoxide dismutase (SOD). This enzyme SOD is useful in removing damaging reactive oxygen radicals. When SOD is inhibited due to hyperglycemia, the lack of SOD can be treated by externally providing SOD mimicking molecules that can remove the reactive oxygen radicals. This form of treatment may prove to be effective in treating diabetic complications.[1]

A third therapeutic alternative is benfotiamine, a thiamine derivative that can help manage the levels of harmful glucose intermediates. This also appears to be a promising therapeutic approach against retinopathy.[1]

Lifestyle modifications besides drug therapy have also been shown to be beneficial in reducing the onset or progression of type 1 and type 2 diabetes. Dietary changes, smoking cessation, group counseling, stress management, and exercise have all been observed to help reduce the onset of microvascular and macrovascular

diabetic complications. A comprehensive overview of 10 human research trials (randomized controlled patient trials) observed a positive effect of various combinations of interventions on diabetes and diabetic complications. In some cases, a positive effect was observed when these interventions were administered in conjunction with anti-diabetic medications.[4,26]

Conclusion

Complications result from long-term diabetes. In order to prevent these debilitating effects, timely screening ought to be conducted in all individuals diagnosed with diabetes. If you wish to avoid serious complications, all warning symptoms must be taken into accounted and acted upon. With new and emerging therapies, there is hope in the fight against diabetes and its insidious counterparts.

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Glycemic Index

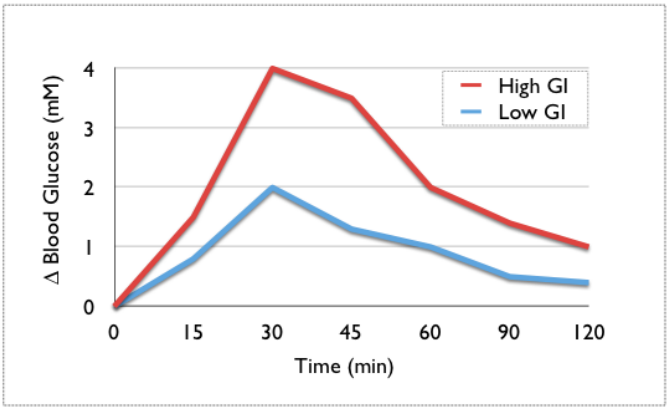
Introduction

A bag of potato chips, a rich piece of chocolate cake, a cup of rice – what do they all have in common? They all contain carbohydrates. Potatoes, flour, and rice are all starchy substances.

Starch is a complex carbohydrate. Wait a minute! What is a complex carbohydrate? Carbohydrates were initially classified as simple or complex, depending on the number of sugar molecules in the chain or structure. A simple carbohydrate, such as sugar, consists of only two molecules: glucose and fructose. In contrast, a complex carbohydrate, such as starch, consists of long chains of glucose.[1]

Starch and sugar provide energy to the body in the form of glucose. This glucose supplies energy to the nervous system, red blood cells, and, in the case of pregnant women, to the placenta and fetus.

Sugars provide nutrients and calories, and are present in vegetables, grain, milk, and fruits. They can also be added to food. Artificial sweeteners are another food



additive, often used as an alternative to sugar. They tend to provide more calories than nutrients. This means that choosing foods based on calories is not always enough, since you must also take into consideration any artificial or added sugars. These additives will increase the calorie intake.[2]

Prior to the 1980s, it was assumed that all simple and complex carbohydrates had the same effect on blood glucose levels in the body.[3] This theory was based on the concept of carbohydrate counting or carbohydrate exchanges. However, not all starchy substances influence blood glucose in the same manner. This is why Alexandra Jenkins introduced the concept of glycemic index in 1981.[3,4]

What is the glycemic index? It is a value that can tell you a great deal about the direction in which your blood sugar is going to swing. The glycemic index, or GI, measures the effect of a food on blood glucose in a specified time interval (normally two hours).[1,3] Thus, a high glycemic index indicates a food that produces high blood glucose levels in that time interval. By contrast, a food with a low GI produces smaller blood glucose levels.

Are you wondering how the glycemic index of a food is actually measured? Typically, when calculating GI, volunteers consume food in a serving size containing 50 grams (about 1.8 ounces) of available carbohydrates. Available

carbohydrates (avCHOs) are carbohydrates that are readily digested, absorbed, and easily metabolized. avCHOs have a greater impact on our blood sugar than carbohydrates in general, because carbohydrates normally include substances that aren't easily metabolized. To approximate the amount of available carbohydrates in a serving of food, researchers measure the amount of carbohydrates and deduct the concentration of fiber in the food portion.

When measuring GIs, volunteers are fed with a specified concentration of the carbohydrate being tested. Changes in blood glucose levels are then measured at periodic time points (15 to 30 minutes), continuing for two hours after the initial consumption of food.[1,3] The change in blood glucose over these two hours is plotted on a curve, allowing the glycemic index of the carbohydrate to be tested.[1,3,6]

But how are these GI numbers applied in everyday life? What do these values really mean to us? Foods with a low glycemic index are digested and absorbed slowly, so they produce a gradual rise in blood sugar. A glycemic value of less than 55 is considered a low glycemic value. Any value that is more than 75 is considered a high glycemic value, while a value between 55 and 75 is considered moderate.[6]

The Harvard Health Publication has published a table with a list of the glycemic indexes different foods. 70 grams of a white bagel, for example, contains a moderate glycemic index of 72. 50 grams of a wheat tortilla proves to be even less of a burden on our blood glucose, with a glycemic index of just 30. Meanwhile, canned tomato juice (250 ml) has a low glycemic index of 38, compared with cranberry juice (250 ml), which has a moderate glycemic index of 68.[6-9]

In the realm of fruits, 120 grams of grapefruit yields the lowest glycemic index of 25, as compared with 60 grams of raisins, with a glycemic index of 64. In vegetables, 150 grams of baked Russett potatoes has an extremely high glycemic index of 111, while 80 grams of carrots has a GI of just 35.[8,9]

Glycemic Load (GL) and Glycemic Impact

Each food affects our blood glucose levels in a distinct manner. As we have seen, glycemic values can help give us a sense of these effects. We have discussed how the glycemic index is calculated: by measuring the effects of a standard concentration of the test carbohydrate on blood sugar. However, we don't normally eat standard concentrations of a carbohydrate, making it difficult to apply the values in the Harvard Health Publication to our real, everyday lives.[6,10,11]

This is why we have *glycemic load.* The glycemic load of a carbohydrate gives the actual contribution of that carbohydrate to blood glucose levels. It takes into account the quality (glycemic index) *and* the quantity of food, and is generated by multiplying the glycemic index by the weight of the test carbohydrate. This value is then divided by 100.

When measuring the effect of a whole diet on blood glucose, the glycemic load takes into account all the ingredients involved. This measure is referred to as the *dietary glycemic load.* When the glycemic load for a particular meal is less than 10, it is considered a low glycemic load, and any value of greater than 20 is called a high glycemic load. A moderate glycemic load is between 11 and 19.

You can also measure the dietary glycemic load of an average day in your life. If the value for a day's food consumption is less than 80, it is considered a low glycemic load. 100 is a moderate glycemic load, and anything greater than 120 is a high glycemic load.[6,10,11]

The *glycemic impact* of food takes into account both the glycemic index and the glycemic load.[6] Therefore, it is preferable to talk about the glycemic impact of food rather than the glycemic index or the glycemic load.

Keep this simple mind when selecting food: aim for the ones with the lowest GIs; in doing so, you will also be choosing food with low GLs.[10]

Different kinds of food have different GI and GL values. Below are listed the GI and GL values for some commonly consumed vegetables, fruits, dairy products, and bread. Use this table as a tool to better understand the effects of processed foods on GI. For example, you will notice that instant oatmeal has a higher GI than regular rolled oats.

GI and GL in different food groups

Food	GI	GL	Serving size (g or ml)
Vegetables			
Baked Russett potatoes	111	33	150 g
Sweet potato	70	22	150 g
Yam	54	20	150 g
Carrots	35	2	85 g
Peas	51	4	80 g

GI and GL in different food groups (continued)

Food	GI	GL	Serving size (g or ml)
Nuts			
Peanuts	7	0	50 g
Salty cashew nuts	27	3	50 g
Beans			
Baked beans	40	6	150 g
Chickpeas	10	3	150 g
Kidney beans (regular)	29	7	150 g
Lentils	29	5	150 g
Fruits			
Watermelon	72	4	120 g
Dried dates	42	18	60 g
Apples	39	6	120 g
Grapes	59	11	120 g
Bananas	62	16	120 g
Raisins	64	28	60 g
Orange	40	4	120 g
Dairy			
Full-fat milk	41	5	250 ml
Yogurt (reduced fat) with fruits	33	11	200 g
Skim milk	32	4	250 ml
Ice cream	57	6	50 g
Cereal			
Oatmeal	55	13	250 g
Muesli	66	16	30 g
Cornflakes	93	23	30 g
Sweet corn on the cob	60	20	150 g
Instant oatmeal	83	30	250 g
Puffed wheat	80	17	30 g

Continued on next page.

GI and GL in different food groups (continued)

Food	GI	GL	Serving size (g or ml)
Grains			
Quinoa	53	13	150 g
Couscous	65	9	150 g
Brown rice	50	16	150 g
White rice	89	43	150 g
White basmati rice	67	28	150 g
Bulgur	48	150	12 g
Bread and cakes			
Pumpernickel bread	56	7	30 g
Baguette	95	15	30 g
Frozen bagel	72	25	70 g
Sponge cake	46	17	63 g
Banana cake without sugar	55	12	60 g
Hamburger bun	61	9	30 g
Juice			
Unsweetened orange juice	50	12	250 ml
Unsweetened apple juice	44	30	250 ml
Gatorade	78	12	250 ml
Snacks			
Hummus	6	0	30 g
Pizza (Pizza Hut)	36	9	100 g
Honey	61	12	25 g
Potato chips	51	12	50 g
Snickers	51	18	60 g
Pastas			
Macaroni and cheese	64	180	32 g
Boiled white spaghetti	46	22	180 g
Cracker and cookies			
Vanilla wafer cookies	77	14	25 g
Rice cakes	82	17	25 g
Graham crackers	74	14	25 g

The Inner Mechanism

So, we now know that a high glycemic index indicates an increase in blood glucose levels. What this actually means is that high-GI foods, such as junk food (pretzels, potato chips, chocolate bars etc.) will immediately boost our energy levels due to the sudden increase in blood glucose levels. This rapid increase in blood glucose levels will then activate beta cells in the pancreas to release insulin. At the same time, the release of glucagon from the alpha cells of the pancreas is inhibited.

Insulin allows absorption of glucose into the muscle, liver, and adipose tissues. This absorption causes a drop in blood glucose. Thus, after blood glucose levels rise rapidly, blood glucose levels drop (hypoglycemia) within two to four hours. This hypoglycemia stimulates the body to generate more blood glucose to maintain and return to the original blood glucose balance; it does this by increasing the level of free fatty acids. This results in a defective glucose tolerance and insulin resistance, together with a feeling of hunger. This hunger prompts us to eat increasing amounts of high GI foods.[4,12]

However, when you eat low glycemic foods, there is a slow absorption of blood glucose from the gastrointestinal tract. Because of this slow increase, the pancreatic cells that release insulin aren't stimulated, and there is a reduced level of fatty acids, plus an increased sensitivity to insulin levels. A low-GI diet also lengthens the duration between hunger bouts, reduces hypoglycaemia during the night in insulin-dependent diabetes patients, and reduces the free fatty acids that accumulate during sleep.

Finally, a low-GI diet reduces levels of free radicals, while the concentration of antioxidants is increased. This has the effect of lowering the oxidative stress in your body. Oxidative stress is another important factor controlling the concentration of blood glucose in the body. In general, diabetes patients show an increase in oxidative stress, and this increases their resistance to insulin.[4,5]

Influencing the Glycemic Index

Foods contain different concentrations of carbohydrates. As a result, foods have different glycemic index values. There are different factors that can affect the glycemic index value of foods, such as their acidity, the thickness of the outer cover of seeds or vegetables, the preparation time, and the processing method. Let us see how these factors influence the glycemic index[6,11]:

Acidity

Fruits, vegetables, and other foods that are high in acid content (e.g. sourdough bread, vinegar-based dips) all have low glycemic indexes. This is because acidity increases the length of time for digestion.[6,11] The GI of sourdough bread (wheat) is 54. Compare this to white bread, with a GI of 73.

The outer coat

The outer covering of seeds acts as an effective barrier against enzymes in the digestive tract. This reduces the breakdown of starch in these seeds, lowering their GI. To illustrate, pumpernickel bread has a GI of 50, while the GI of a bagel is 72.[6,11]

Preparation time

When you cook foods for longer, you are increasing the chances of absorbing the starch from the food. Longer cooking times break down the starch, facilitating easy absorption. This can be avoided by cooking the food for a shorter time. Spaghetti noodles, when prepared al dente (10 to 15 minutes), have a lower GI (44) than overcooked spaghetti, which has a GI of 64.[6,11]

Choice of food

The glycemic index of a meal is the average of the glycemic indexes of all the different ingredients in the meal. Therefore, a meal containing potatoes and rice, for example, ought to be complemented with beans or leafy vegetables, which have lower GIs.[6,11]

Method of preparation

Highly processed foods contain high GIs, compared with foods that aren't processed to the same extent. For example, microwave meals or ready-to-eat meals have a higher GI than an equivalent home-cooked meal. Indeed, the GI of unprocessed steel-cut oats is 55 instead of 79 for processed instant oatmeal.[6,11]

Viscous fiber

If a food is high in soluble or viscous fiber, its GI tends to be low. Foods such as beans are high in viscous fiber content. High viscosity reduces or delays the action of digestive enzymes on the starch in foods. This has the effect of delaying the rise in blood sugar following food ingestion. To illustrate, the GI of an apple is 40, while the GI of whole wheat bread (higher viscosity) is 73.[6,11]

The addition of fat or protein

The GI content of food is reduced in the presence of protein or fat, since fat and protein prolong starch digestion. For example, when potatoes are combined with chicken or cheese, their glycemic indexes are reduced.[6,11]

Difference in starch

Differences between starches influence the GI of foods. Amylopectin is the predominant starch in foods; it is digested rapidly and has a high GI. High-gluten rice and starchy potatoes both contain amylopectin. In contrast, foods with low GIs, such as leafy vegetables and beans, tend to consist of amylose, which is digested slowly.[6,11]

The type of sugar

Two of the major sugar molecules in the human diet are fructose and glucose. In starch, the major constituent is maltose, which consists of two connected molecules of glucose. As an example, Raisin Bran cereal (richer in fructose and glucose) has a GI content of 61, compared with Rice Krispies (higher in maltose), which has a GI of 82.[6,11]

Glycemic Control

What is glycemic control? The glycemic index influences three factors in the body: glycated hemoglobin, blood glucose concentrations after a meal (postprandial glucose), and blood glucose concentrations while fasting.[4] Good glycemic control amounts to bringing all three of these factors into balance.

Postprandial blood glucose

Measuring the levels of blood glucose after a meal is one way to evaluate glycemic control. A low-GI diet has been shown to be associated with lower blood glucose levels. Although some studies that suggest a low GI has little effect on blood glucose, fewer blood vessel complications are seen with a low-GI diet. This is beneficial in preventing the onset of diabetes. A high-GI diet increases the concentration of blood glucose with an increase in blood vessel complications. Don't forget, there is an increased concentration of free radicals with a high-GI diet, which are factors that influence the onset of diabetes.[4]

Fasting blood glucose

Several research studies have shown that a low-GI diet can significantly reduce the fasting blood glucose levels.[4]

Glycated hemoglobin (HbA1c)

There is research data that indicates that there is a reduction in glycated hemoglobin levels with a low-GI diet. However, other research studies have not observed a compelling effect of low-GI diets on HbA1c, one of the measures of glycemic control.[4]

The Link Between Glycemic Index and Diabetes

When the sensitivity to insulin is increased, and the demand for insulin is reduced, the incidence of diabetes type II is reduced. But an increased glucose level (hyperglycemia) reduces the functioning of the β-cells of the pancreas. A high GI diet increases the blood glucose levels as well as the insulin levels. These are

responsible for the development of diabetes. On the other hand, a low GI diet will result in lower blood glucose and insulin levels.

As mentioned earlier, foods with a low glycemic index are metabolized slowly, resulting in a delayed release of insulin. This diet appears to be favorable in preventing the onset of diabetes. There are studies that support this assumption. The rate of carbohydrate absorption is decreased with low GI foods since the fiber content is high in such foods. When low GI foods are consumed, the absorption of glucose is very slow, and the free fatty acids are suppressed by the body. The concentration of blood glucose is low, and there is a reduction in the insulin levels. Over time, the blood glucose concentration returns to the baseline level.[5]

High glycemic index foods are rapidly metabolized, and insulin is released at a rapid rate. This increased insulin leads to a reduced expression of insulin receptors in various cells in the body, which results in enhanced resistance to insulin. Furthermore, a functioning error in the pancreatic B cells develops. This accelerates the onset of diabetes. Diabetes results from an increase in blood glucose and an increase in insulin levels. In addition, the physical fitness of an individual, and genetics are other contributing factors. Individuals with low physical activity and overweight individuals are affected by the glycemic index more than those without these risk factors. Thus, high GI foods can accelerate the effects of diabetes based on the diet, genetics, and the physical fitness of individuals.[5]

While the science behind the increase or decrease in insulin has been explained, it is still not clear if the glycemic index actually influences the occurrence of

diabetes. Research studies are still trying to find a decisive link between the glycemic index and resistance to insulin.

A rise in the incidence of diabetes has been observed in populations (e.g., Australian Aborigines, Indians, Pima-Indians) that traditionally consumed low GI foods. The increase in affluence in many of these populations has increased their access to high GI diets. This change in diet has increased the incidence of diabetes in these populations.[5]

Effects of Planning Your Meal with the Help of GI

A systematic review of studies that used the GI to select carbohydrate-linked foods has shown that a low GI-diet has a significant effect in reducing total cholesterol in diabetic patients. Another study demonstrates that a low GI-diet is an efficient way in reducing the risk of complications, reducing the number of medications and doses, as well as improving the quality of life in patients with diabetes. The level of glycated hemoglobin A1c levels can be lowered with a low glycemic index diet. Additionally, episodes of hypoglycemia are also reduced with a low glycemic index diet.[13]

Effects of Sleep on GI

Did you know that GI has an association with sleep patterns in diabetic patients? The duration of sleep and the pattern of sleep contribute significantly to the development of glycemic variability and affect the glycemic control of patients with Type 1 diabetes. It has been reported that patients with Type I diabetes show

variable sleep patterns. These variable sleep patterns can result in insulin resistance in Type I diabetes patients. Similarly, studies have noted that the glycemic index is affected in Type 2 diabetics who suffer from insufficient sleep. Research has noted that poor glycemic control in individuals correlates with disturbed sleep, such as frequent periods of arousal and awakening. Insufficient sleep causes activity in the sympathetic nervous system and the adrenocortical system, as well as increases insulin resistance. These changes affect glycemic control.[14]

Foods that Influence GI

Cinnamon performs the same function as insulin. Cinnamon can increase the uptake of glucose into the skeletal muscles and adipocytes. Cinnamon also has a favorable effect on the glycemic control of your body.[15]

A research study analyzed the effects of sweetened beverages and observed that such beverages increase the glycemic load in individuals.[16] As well, cereals, bread, and starchy foods increase the glycemic load in individuals. Noncaloric sweeteners were observed to reduce the body mass index and the energy intake of individuals. Fructose in the diet was found to reduce the blood glucose levels in diabetic patients. Although sweeteners have been shown to

influence the glycemic index, the results of the study on artificial sweeteners need to be confirmed with more rigorous clinical studies.[17]

Glycemic control can also be of benefit in cardiovascular disease. A study showed that intensive glycemic control therapy could reduce the risk of cardiovascular disease and myocardial infarction in type 2 diabetes individuals. However, in obese individuals, such intense therapy could have a negative effect on mortality, stroke, and heart failure. Intensive therapy involves a combination of drugs, such as metformin, insulin, sulfonylureas, and pioglitazone.[18]

Studies have also found that eating a low-carbohydrate diet showed reductions in weight and glycated hemoglobin levels in diabetic individuals.[19,20]

Benefits of Consuming Low GI Foods

Okay, we have seen how to calculate the glycemic index, but what do we gain by eating foods with a low glycemic index?. We know that glycemic index is connected to our blood sugar and in turn, to diabetes. Diabetic patients are advised to consume a diet that is low in GI since it reduces hypoglycemia and glycemic variability. Additionally, there is a lower risk of heart disease when low GI foods are consumed as cholesterol levels also become reduced. Of course, the most attractive feature of consuming low GI foods is that it gives you greater control over your appetite because it helps you manage cravings better.

Low GI foods are recommended to prevent the onset of diabetes. Let us see how low GI foods pose an advantage in preventing that onset. It has been observed that low GI foods help to improve glycemic control.[21] This helps in preventing

cardiovascular disease. The high fiber content of a low GI diet prevents the synthesis or the re-absorption of cholesterol. In addition, hyperinsulinemia and hyperglycemia are reduced in a low GI diet. This avoids the complications of diabetes.

In a comprehensive analysis of the research data on glycemic index and glycemic control, The European Association for the Study of Diabetes recommends that individuals should replace a high GI diet with a low GI diet.[22] The American Diabetes Association recommends that low GI foods can reduce excess blood glucose.[11,22] A low GI diet can lead to improvement in glycemic control. However, it is not known whether it can be effective in preventing diabetes.[22]

When we talk about a low GI diet, we are talking about replacing food made with potatoes or white flour with whole grain foods or cereals. Whole grain foods or cereal have been shown to be effective in reducing the incidence of diabetes. Foods that come under the category of a low-GI diet include lentils, peas, beans, cereal, parboiled rice, bulgur, oats, bran, barley, pumpernickel, and pasta.[23]

The GI of foods can be modified based on the combination of the food chosen. For example, high GI potatoes may be replaced with yams or sweet potatoes. Avoid desserts, such as ice cream, cakes, and pastries. Instead, yogurt, nuts, may be consumed with high GI food to counteract and lower the GI. A high GI diet of cereal can be modified to a low GI diet with cinnamon, berries, flaxseed, and nuts.[23]

The Ideal Diet

The ideal diet should include whole grain cereals. A dietary guideline for Americans recommends that 14 grams of fiber should be consumed for every 1000 calories. Whole grain cereals should account for half the cereal diet. Around 3 cups of fat-free or low-fat milk should be included in the diet. Approximately 2.5 cups of vegetables and 2 cups of fruits (~2000 calories) should be consumed daily. This type of diet represents a low GI meal plan. Low GI foods can regulate the glycemic load (GL). However, large portions of a low GI diet need to be consumed. On the other hand, smaller portions of high GI foods can regulate GL.[23]

A low-GI diet shows promise in controlling the onset of diabetes. In terms of health economics, following a low-GI diet would be economically feasible. Research studies are trying to confirm the utility of low-GI diets in preventing other complications of diabetes, such as cardiovascular disease. One thing is clear, modifying your dietary lifestyle is necessary if you want to live a long, healthy life. I am optimistic that this article will provide you with the necessary resources and inspiration to change your dietary lifestyle. So, let's start living a glycemic-controlled healthy life!

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Exercise

Did you know that physical activity and cardiovascular fitness are linked to significantly lower rates of morbidity and mortality for people both with and without diabetes.[1] Just consider the benefits of exercising: stress relief, a boost in energy, weight control, and a better night's sleep. Exercise is not only fun, but by remaining active, you are helping yourself to stay healthy and happy. Exercise is also a something of a panacea, in that it promotes a fitter body, a sharper mind, and a stronger overall well-being.

Unfortunately, we have never been less fit as a society. This is largely a product of the times: technology has made our lives less labor-intensive. Consequently, we are less active, and obesity and diabetes are on the rise. It's a weird and wonderful world we now inhabit – a science fiction universe where you're more apt to play a sport virtually, on a couch, than to physically engage in the real-life activity. Even the work we do is less physically demanding than labor in the past, as many arduous tasks are now carried out by machines. Every facet of our lives is becoming less laborious, from everyday chores around the house to shopping. The effect of all this a reduction in the amount of physical energy exerted during the course of your day. Therefore, it’s no wonder that our waistlines continue to

expand and that obesity and diabetes rates are growing exponentially. We move around less and burn off much less energy than our predecessors.

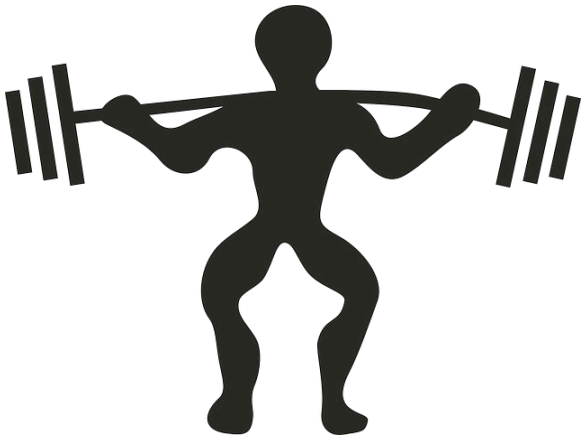
The fact is, regular physical activity helps your body's systems to function better, and it keeps a host of diseases, including diabetes, at bay. According to the 2008 Physical Activity Guidelines for Americans, being physically active on a regular basis is the key to losing excess pounds and maintaining a healthy weight.[2] And although there is no such thing as a guarantee of good health, combining a healthy, nutritional diet with a regular regime of exercise comes pretty darn close. Exercise is not a fad or a snake oil remedy; the scientific evidence overwhelmingly indicates that regardless of your age or current physical condition, being physically active leads to a more enriched, healthier life.

The importance of staying physically active is especially pronounced when it comes to diabetes. If your body fails to create enough insulin or if you are insulin-resistant, physical exercise can make your body become more insulin responsive; it can also burn off more calories, trim off excess weight, reduce the risk of heart disease and stroke, and help you stabilize your mood.[1,2]

It's easy to enjoy the benefits of exercise in a way that is fun and suited to your lifestyle – whether it's walking, running, hiking, dancing, surfing, going to the gym, swimming, playing golf, taking yoga, or joining a team sport. Find an activity that suits you. Regardless of the specific activity you choose, there are several

universally applicable tips to help you plan an exercise regime. These will be discussed below.

Tips



1. Ask your doctor for advice. Before beginning a rigorous exercise program, diabetics should be assessed for conditions that might be exacerbated by robust physical activity. Your physician will take into account your health history and will advise you on the best type of exercise for someone in your condition. They may then make changes to your insulin program as the effects of exercise improve your overall health.[3]

2. Pick an activity you enjoy. When it comes to exercise, the gym isn't your only option. Finding activities that you enjoy will help ensure that you stay motivated and active. You can pick new exercises, or activities you enjoyed in the past. Dancing, golf, yoga, skipping, walking, and swimming are just a few ideas. Anything that elevates your heart rate is a step in the right direction.

3. Go slow. If you haven't been active for some time, ease into your new exercise routine with 10 minutes of exercise at a time, slowly working towards 30 minutes a day.

4. Monitor your blood sugar. If you plan to work out for more than an hour, check your blood sugar levels before, during, and after your workout, to determine whether you need to make adjustments.

5. Keep some carbs at hand. Always carry a small snack while exercising, just in case your blood sugar gets low.

6. Add a couple of sessions of strength training. Adding resistance workouts to your exercise regime can do wonders for blood sugar control. Diabetics benefit from both aerobic and resistances exercises, and get the most bang for their buck by combining both types of training. The recommended amount of aerobic exercise per week is 150 minutes, combined with at least three sessions of resistance training.[1]

7. Ritual behavior. When you exercise, eat. And take your medicines at the same time every day - the habitual routine helps to regulate blood sugar and prevent hypoglycemia.[4]

8. Make it a collective effort. When you work out with someone who knows what to do if your blood sugar gets too low, it takes a lot of the worry out of the equation. It can be more fun, too. However, if you prefer solo exercise sessions, it's better to be safe than sorry, so be sure to wear a medical identification tag.

9. Foot care. Wear proper athletic shoes and be sure to monitor your feet. If you do notice foot problems, make sure you contact your doctor.[1]

10. Hydrate. Drink water before, during, and after exercise.

11. Know when to apply the breaks. Mildly aching muscles are normal. However, sudden pain is a warning sign to slow down. Keep in mind that the likelihood of injury decreases if you build up slowly towards increasingly demanding workouts.

Exercises to Avoid When You Have Diabetes

Although regular physical activity is an essential component of a healthy lifestyle, there are situations where your diabetes may not allow you to do certain exercises. The following complications may require special attention when planning your exercise routine:

Proliferative diabetic retinopathy (PDR) is a condition characterized by the growth of new blood vessels in the retina. These new blood vessels are often thin and fragile and can easily leak blood. If you have PDR you should avoid strenuous and high-impact activities. Having your head in an inverted position for long periods of time is also another thing to avoid.[5,6]

Diabetic peripheral neuropathy is a long-term diabetes complication that causes damage to the peripheral nerves in the toes and feet, resulting in loss of sensation.

Repetitive exercise on feet that have lost their sensitivity may lead to ulceration and fractures. So do your feet a favor: check your feet often and avoid high-impact exercises that may further damage your feet.[1,6,7]

Advanced kidney disease. Diabetes damages the small blood vessels in the body. When the blood vessels in the kidneys are injured, this organ becomes incapable of adequately filtering out impurities from the blood. Diabetics with advanced kidney disease can engage in moderate-intensity activities, such as walking, but should avoid strenuous activity.[6,8]

High blood glucose levels. If your blood glucose levels are higher than 250 mg/dl and ketones are present in your urine, you should avoid doing exercise. The presence of ketones indicates that you don't have enough insulin and that you may be at risk of ketoacidosis, which can lead to serious complications. You are also at risk for ketoacidosis and dehydration if glucose levels are higher than 300 mg/dl. At these levels, it is best to wait until your blood sugar drops to a safe range of between 100 to 250 mg/dl.[9] Therefore, check your blood glucose before, after and possibly during physical activity to ensure your blood glucose falls within an appropriate range.

To wrap up, successful management of diabetes involves eating right *and* exercising. Exercise not only helps to improve your blood sugar control, but also reduces your risk of heart disease and stroke. So, don't think twice: get off the couch and begin experiencing the joys and health benefits of a regular exercise routine.

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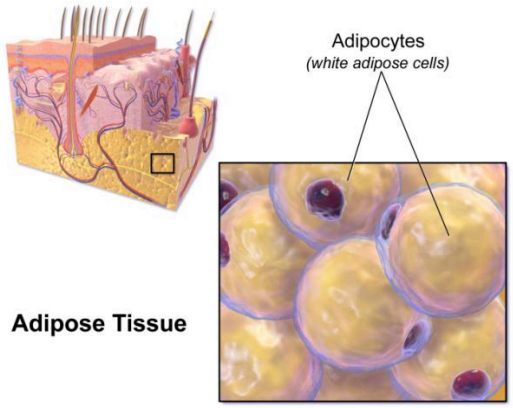
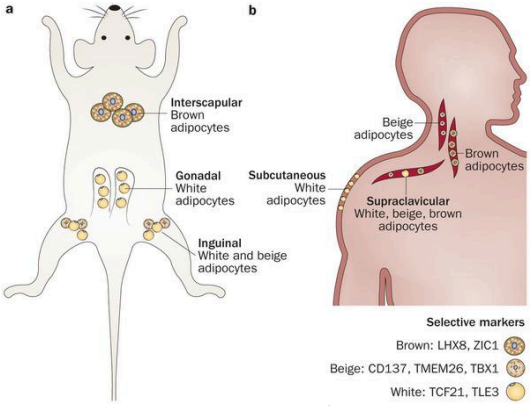
Brown Fat and Diabetes

In the following chapter, we are literally going to be turning down the heat. By cooling down your body, you can stimulate the production of brown fat and start burning off the extra weight that puts so many people in jeopardy of developing type 2 diabetes. The fact that even fat can be healthy may sound farfetched, but seriously… the benefits of brown fat CAN BE enormous. Read on to discover more.

Introduction





Obesity and type 2 diabetes are two conditions that are closely tied together, giving rise to the term "diabesity," coined to represent their interdependent relationship.[1] Bear in mind that both weight gain and a sedentary lifestyle are major contributors to type 2 diabetes. Carrying excess weight stresses your body into a chronic state of inflammation that can lead to insulin resistance - a precursor of type 2 diabetes.[2,3] It is no coincidence that the worldwide number of type 2 diabetes cases increases at the same rate as the obesity epidemic, prompting the development of new treatment options that address both conditions.[4] To this end, programs focused on the intervention and prevention of type 2 diabetes involve

direct measures to reduce the global problem of obesity, including the promotion of a healthy diet, healthy weight, regular physical activity, and smoking avoidance.[2]

In recent times, there has been a burgeoning interest in the biology of adipose (fat) tissue, to better understand the mechanism by which fat affects obesity and related metabolic disorders, such as type 2 diabetes.[5] Adipose tissue consists of fat cells (adipocytes), and is found in specific locations in the body.[5] Mammals produce two main types of adipose tissue. White adipose tissue (WAT) is the best known of the two; it stores fat molecules, excess amounts of which can lead to weight gain and obesity.[6] Brown adipose tissue (BAT), or brown fat, is derived from muscle, and is involved in the burning of energy to generate heat - a process referred to as thermogenesis.[6]

Burning energy to generate heat sounds abstract; however, the study of brown fat has led to breakthroughs in the treatment of metabolic diseases via the exploitation of thermogenesis. Metabolic disorders, such as type 2 diabetes, are centered around imbalances between food (energy) intake and energy expenditure. In the case of obesity, energy intake exceeds energy expenditure, leading to the storage of excess fat and weight gain.

However, brown fat cells can combat this process, by helping to burn stored energy for heat production.[7] Therefore, BAT is considered “good” fat, due to its inverse relationship with body mass index (BMI). More brown fat is found in lean people than in overweight people.[6]

As a result, brown fat has gained considerable attention for its therapeutic potential as an anti-diabetic tissue. Thanks to continued research focused on brown fat cell development and function, we now know of several molecular factors and pathways that may be exploited as targets for novel weight loss and diabetes treatments.

Brown Fat: Feel the Burn

Brown adipose tissue (BAT) is identified as a specialized, heat-producing (thermogenic) organ that allows small mammals, including human newborns, to survive in cold conditions.[8,9] When we feel cold, we initially generate heat by shivering. However, when you are exposed to cold temperatures for longer periods of time, heat generation is switched to non-shivering thermogenesis by BAT.[10] Your sympathetic nervous system will sense cooler temperatures and initiate BAT activation by releasing a hormone called *norepinephrine*, which targets specific receptors on the surface of brown fat cells. This starts a cascade of events that not only increase the expression of thermogenic genes, but also lead to *lipolysis* – the breakdown of fats.[8] Lipolysis releases free fatty acids (FFA), which activate uncoupling protein-1 (UCP1), a molecule unique to the mitochondria of brown fat cells. Mitochondria are the energy-producing structures in the cell, sometimes referred to as the "powerhouses." The chemical energy normally produced in mitochondria is

dissipated by the activity of UCP1 and converted into heat.[5] UCP1 also permits the use of fatty acids and glucose to produce heat, thus influencing glucose and fat metabolism.[5,8]

Our understanding of brown fat is based on several rodent studies, which noted the importance of BAT in the rodents' metabolism.[8] Mice that lack BAT have reduced energy expenditure, are susceptible to diet-induced obesity, and are insulin-resistant.[5,8] By contrast, mice that received BAT transplants lost weight, and improved their blood-glucose control and insulin sensitivity, demonstrating that BAT has the potential to help people with metabolic syndromes.[4]

Human newborns have high amounts of BAT in their bodies, used for thermoregulation. Until recently, the physiological relevance of brown fat in adults was not emphasized, and it was thought to have less functional importance in maintaining body temperature than cognizant behavior (e.g. wearing layers and staying close to a heat source).[11] BAT levels appeared to regress as humans grew into adulthood, having negligible effects on energy regulation in the adult body.

However, the idea that adults had no BAT was dispelled in 2009 by three seminal studies that detected active BAT in adults.[8] These studies used the radioactivity-based imaging technique known as positron emission tomography (PET).

A combination of positron emission tomography (PET) and computerized tomography (CT)allowed researchers to detect active BAT, indicated by the presence of UCP1 and the ability of the tissue to take up glucose under cold conditions.[12,13] BAT activity was shown to be more prevalent in women than in

men, and differed between men, such that BAT levels were higher in young men, and lower in men who were overweight or obese.[14]

It has now been shown that brown fat cells in BAT can burn excess energy (calories) into heat. This process limits the storage of excess calories as fat, with downstream benefits on glucose tolerance, fat metabolism, and body weight.[15]

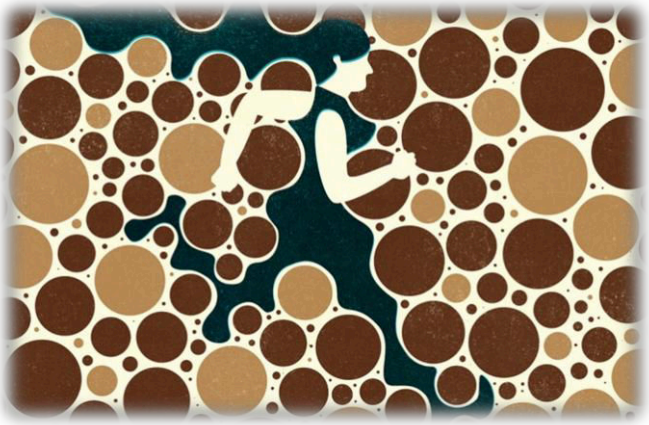
Other factors influencing the presence of active BAT are external temperature, body mass index, and diabetes status (a non-diabetic status was associated with more active BAT).[9] Although BAT activity appears to decrease with age, it probably retains a functional role in thermoregulation in cold weather, with maximal BAT activity in the winter.[8,9] Nonetheless, lower quantities of active BAT with age may explain why it's easier to accumulate body fat as one grows older.

A small study has looked at levels of BAT among people of different ethnicities, providing some insight into why certain populations may be more susceptible to type 2 diabetes than others. South Asian people, for instance, have a higher risk of developing type 2 diabetes than Caucasians, and they also possess lower amounts of metabolically active BAT (32% lower than the Caucasians).[15]

Beige Cells: Browning the White Fat

The last few years of BAT research have uncovered an additional type of thermogenic tissue that can arise from white adipose tissue; the cells in this tissue are called beige cells. Beige, or brite (brown in white), fat cells are found sporadically throughout white fat tissue and act as brown-like fat cells when

exposed to external cues, such as chronic cold conditions.[10] Animal studies have shown that this conversion can also be induced by certain chemical compounds, such as β3-adrenergic agonists, which bind to fat cell receptors and lead to thermogenesis.[8] The conversion from white to brown, referred to as "browning", depends on increasing UCP1 content; UCP1 is found at consistently high levels in brown fat cells but at relatively low levels in beige cells, until induced by stimuli.[8,16]



These inducible brown cells originate from a distinct cell lineage from that of classic brown cells. It is now known that beige cells make up the thermogenic tissues that contribute most to the BAT activity in adults.[8,10] Having two types of thermogenic fat tissue expands our prospects of developing different therapies, since it provides two separate targets for intervention.[8]

BAT for Therapy

BAT provides an alternative approach to obesity treatments and type 2 diabetes, by allowing us to focus on manipulating adipose biology, instead of reducing calorie intake or removing fats through surgery.[5] Nascent BAT treatments aim to boost the amount or activity of brown fat tissue, thereby protecting against body fat accumulation and type 2 diabetes.[5] The conversion of white fat into beige fat is an area of intense interest, as the transformation of existing fat cells is a more

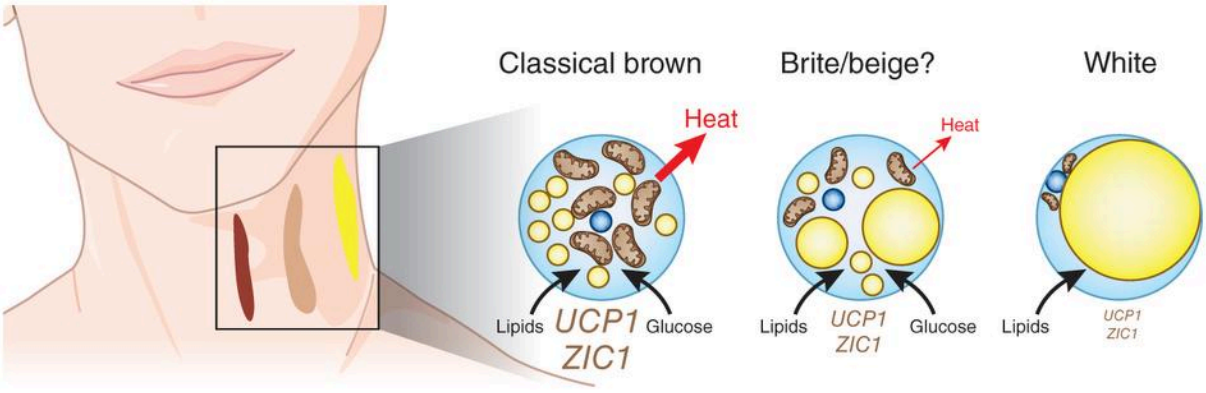
plausible future option than brown fat transplants. However, the ultimate goal should be to build and maintain classical brown fat stores throughout life, and notto produce them from another cell source.[17]

BAT has been shown to increase in response to repeated exposure to cold temperatures and the ingestion of certain food ingredients.[18] One study in particular noted the potential ability of cold therapy to increase BAT activity in the form of beige cells. Healthy men were exposed on a daily basis to temperatures of 17 ^{o}C for 2 hours over the course of 6 weeks. This led to increased BAT activity, even in those who had no detectable BAT at week 0.[10] Importantly, this increased BAT was associated with a reduction in body fat mass. Alternatively, BAT can be activated by immersing a hand in cool water at 20 ^{o}C.[8]

Further support comes from a study showing that beige fat levels are higher in winter than in summer.[19] Indoor heating, and our aversion to staying outdoors in colder weather, replace our body's natural ability to maintain warmth; indeed, greater BAT activity can be induced simply by turning down the thermostat for a few hours a day.[20]

While exercise remains the most effective means of burning calories and fat, new interventions for activating and expanding BAT would help individuals who are unable to engage in physical activity. BAT-derived therapeutics using cold protocols are as appealing as they are safe. Turning down the heat is both economical and effective, with results comparable to those of exercise.[8]

In addition to cold stimuli, "browning" stimulators are under study for the enhancement of BAT activity. One of these is capsaicin, the pungent "hot" ingredient found in chili peppers; there is evidence that capsaicin can be effective in stimulating BAT thermogenesis. For example, capsinoid – a non-pungent capsaicin-related compound – has been tested as an alternative to cold treatment. Studies show that ingesting capsinoid on a daily basis can increase BAT thermogenic activity; in these cases, weight loss seems to be the most significant in individuals treated for a longer time period who were already overweight.[10,21] More recently, the benefits of capsinoid were shown to complement the benefits of exercise. In animal studies, mice fed on a high-fat diet also received capsinoid supplementation combined with exercise, resulting in enhanced fat loss and weight loss compared with just exercise alone.[22]



The search for drugs capable of increasing BAT function is currently focused around the signaling pathways of BAT, and targets molecular factors serving as potential therapeutic targets. These molecules include hormones and growth factors that regulate BAT activity, such as orexin. Orexin is a brain hormone that promotes feeding, sleep/wake cycles, and physical activity; it is also implicated in brown fat thermogenesis. Orexin studies in rodents show that a deficiency in this

molecule leads to decreased energy expenditure, along with increased weight gain and fat tissue.[23]

Molecular factors that activate the "browning" process also include hormones, such as irisin and apelin, along with bone morphogenetic proteins (BMP7 and BMP8B).[8,24,25]. Finally, recent advancements in mouse models have aided in the search for new drugs that enhance BAT activity, including ThermoMouse, which screens for pharmacological agents that can enhance UCP1 levels, thereby boosting thermogenesis.[26]

Conclusion

While BAT represents an exciting prospect in the treatment of type 2 diabetes and obesity, it's unlikely that we will see these new drugs in clinical practice for some time. However, there is some appeal in revisiting previous drugs that have already been used for weight loss, but with a new design focused on BAT activity. For example, β3-adrenergic agonists are a class of agents capable of inducing the "browning" effect on white fat tissue.[8] Prior to the discovery of BAT activity in adults, β3-adrenergic agonists were used as a treatment for weight loss with limited success (due to short-term, nonspecific effects). Now, with advanced knowledge of specific pathways involved in BAT activity, these agents are being revisited with specific targets in mind, combined with efforts to enhance their durability in the body.[8]

One β3-adrenergic agonist drug has already shown promise in boosting BAT for the treatment of type 2 diabetes and other metabolic disorders.[27] This drug was

approved to treat overactive bladder but was also shown to stimulate BAT activity, increase glucose uptake, and enhance the resting metabolic rate in healthy men after a single dose (27). However, further research is necessary to understand whether this drug will be a viable and safe option for the future treatment of obesity and type 2 diabetes.[28]

While all the research data indicate that promoting brown fat activity in your body may be a promising approach in combating diabetes and obesity, more evidence is needed to verify its risks and benefits. So let's keep our eyes out and our fingers crossed.

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Antioxidants and Diabetes

Introduction

Oxygen is a double-edged sword. On the one hand, you need it for critical body functions, such as breathing and the immune response. However, under certain circumstances, its reactive chemical nature can damage your body's cells and tissues. In recent decades, research has shed light on oxidative stress, an imbalance related to the amount of oxidation in the human body. Oxidation takes place when body cells interact with highly reactive oxygen-containing molecules, known as reactive oxygen species or ROS. Although it is a natural bodily process, oxidation can inflict damage to your cells when it occurs in excess. Factors that can increase ROS levels and trigger oxidation include UV radiation, stress, and cardiovascular disease.

Although oxidative stress is closely linked to the development of diabetes, the good news is that your body produces antioxidants to combat excess oxidation. Some antioxidants, such as alpha-lipoic acid, are produced in sufficient quantities by the body and needn't be consumed as part of one's diet. However, Vitamins A, C, and E must be obtained from dietary sources in order to preserve good health.

Throughout this chapter, we will be exploring antioxidants other than Vitamins A, C, and E, which will all be discussed in the vitamin chapter. These non-vitamin antioxidants include alpha-lipoic acid, co-enzyme Q10, and resveratrol. There is increasing scientific evidence that these molecules have beneficial effects on insulin resistance and beta cell dysfunction.[1-3] However, it is unclear whether or not antioxidant activity is responsible for these effects; while these non-vitamin molecules have proven antioxidant efficacy *in vivo* (in the lab), they do not have proven antioxidant efficacy in the human body. So while it is likely that these molecules are beneficial for diabetics, we are still not sure whether they are truly 'antioxidants.'

For now, we will continue to refer to the molecules discussed in this chapter as 'antioxidants' based on the results of animal and lab studies. Future human investigations may one day decide whether or not these labels are accurate.

Alpha-Lipoic Acid

Alpha-lipoic acid (LA) is one of the most effective ROS scavengers. Synthesized in the human liver, it plays an important role in generating energy from glucose. It is also taken as a supplement for its alleged antioxidant properties. Specifically, it is thought to increase levels of the antioxidant glutathione, promote anti-inflammatory activity, and combat oxidative stress.

LA is used in Western medicine for the treatment of peripheral diabetic neuropathy. In controlled clinical trials, it has been observed to significantly

improve symptoms of diabetic neuropathy when administered both orally and intravenously; it was also found to be both safe and well-tolerated.[4-8] These positive results were confirmed by a recent meta-analysis of fifteen clinical studies, which analyzed intravenous treatment with LA over 2-4 weeks. Nerve conduction velocity and the symptoms of diabetic peripheral neuropathy were considerably enhanced during LA treatment.[9]

LA has also been found to improve insulin sensitivity and glucose control.[10-12] This has been demonstrated using several different LA delivery methods. For example, a number of clinical studies have reported an improvement in insulin sensitivity and the metabolism of glucose in type 2 diabetic patients following continuous intravenous infusion of LA.[13-16] The oral delivery of LA also yields a significant effect on insulin sensitivity, albeit on a smaller scale.[17,18]

Oral delivery of LA can be carried out using one of two different methods: controlled or uncontrolled. Both have been tested with positive results. With controlled delivery, the LA is released into the bloodstream at a slower rate, reducing the need to take the supplement at frequent intervals. Controlled-release LA delivery was found to be safe and well-tolerated, while significantly reducing levels of fructosamine (a measure of glucose concentration) in the plasma of type 2 diabetes patients.[19] Meanwhile, non-controlled (immediate) release of LA has been reported to enhance insulin-mediated glucose disposal in type 2 patients.[20]

Anyone considering LA supplementation should be aware of an autoimmune condition known as Hirata Disease, which predisposes affected individuals to hypoglycemia if they are on lipoic acid supplements.[21] Therefore, speak to your doctor before beginning any regime involving LA.

Dietary Sources

Lipoic acid is currently prescribed in 600-1200 mg/day doses for treating type 2 diabetes.[22] It can be found in a variety of food sources. The Linus Pauling Institute at Oregon State University reports that kidney, heart, liver, spinach, and broccoli are all rich in lipoic acid. Lipoic acid is also found in lower amounts in tomatoes, peas, and Brussels sprouts.[23]

Drug Interactions of Lipoic Acid

It is important to be aware that LA interacts with diabetes medications. Since diabetes medications and lipoic acid can each lower blood sugar on their own, taking lipoic acid in conjunction with diabetes medications can cause blood sugar to drop too low. However, more evidence is required to establish whether this interaction is large enough to be a cause for concern.

It has been speculated that antioxidants such as lipoic acid may decrease the efficacy of some cancer medications. Therefore, consult with your doctor before taking lipoic acid supplementation.[22]

Co-enzyme Q10

Found naturally in the mitochondria of cells, co-enzyme Q10 is a potent antioxidant. It is being considered as a potential treatment for a host of conditions, including diabetes, heart disease, elevated cholesterol levels, and elevated blood pressure.

In the realm of diabetes research, a double-blind, placebo-controlled study concluded that CoQ10 could reduce plasma levels of glucose and insulin in patients with coronary heart disease, suggesting that it might improve insulin sensitivity.[24] Another randomized, double-blind, placebo-controlled study found that co-enzyme Q10 can reduce levels of glycated hemoglobin (HbA1c) in type 2 diabetes patients. This study also observed decreased levels of total cholesterol and LDL cholesterol ('bad' cholesterol) in patients taking co-enzyme Q10. However, in another study, no differences in triglycerides, fasting plasma glucose, and HDL ('good' cholesterol) were found between patients taking co-enzyme Q10 and patients given a placebo.[25]

Therefore, despite thus far encouraging results, further research is required to clarify the true efficacy of co-enzyme Q10 in diabetes treatment.

Dietary Sources

Rich sources of CoQ10, include meat, poultry, and fish, as well as soybean, canola oils, and nuts.[26] See the following table for a more detailed comparison of the CoQ10 content of different foods:

Dietary Sources of Co-enzyme Q10

Food	Serving	Coenzyme Q10 (mg)
Beef, fried	3 ounces	2.6
Herring, marinated	3 ounces	2.3
Chicken, fried	3 ounces	1.4
Soybean oil	1 tablespoon	1.3
Canola oil	1 tablespoon	1.0
Rainbow trout, steamed	3 ounces	0.9
Peanuts, roasted	1 ounce	0.8
Sesame seeds, roasted	1 ounce	0.7
Pistachio nuts, roasted	1 ounce	0.6
Broccoli, boiled	½ cup, chopped	0.5
Cauliflower, boiled	½ cup, chopped	0.4
Orange	1 medium	0.3
Strawberries	½ cup	0.1
Egg, boiled	1 medium	0.1

Source: National Institute of Health (27)

Drug Interactions of CoQ10

CoQ10 supplements have been observed to lower the effect of Warfarin, an anticoagulant used to slow blood clotting. Please consult your doctor if you are taking Warfarin and are considering CoQ10 supplementation. If you are on blood pressure medications, be wary of taking extra CoQ10, as evidence suggests that CoQ10 can lower blood pressure further. There is also some speculation that antioxidants such as CoQ10 may decrease the efficacy of some cancer medications.[27]

Resveratrol

Resveratrol is part of a group of plant compounds called polyphenols. These compounds are believed to have antioxidant properties that protect the body against damage linked to cancer and heart disease.

This antioxidant was discovered after an attempt to answer an interesting health-related question: why do the French have such low rates of cardiovascular disease? This question became a paradox when you took into account the higher-than-average consumption of saturated fats in France, such as cheese and butter.

Scientists wondered if some clues to this paradox might be found in another distinctly French behavior: the country happens to be the home of some of the highest per capita wine drinkers in the world. Once investigators began focusing on wine as the key to French cardiovascular health, it wasn't long before they had their first molecular candidate: resveratrol.

Resveratrol is a compound found in high concentrations in red wine (0.1-14.3 mg/l).[25] It has a lengthy list of associated benefits, including anti-cancer activity, cardioprotective activity, antioxidant and glutathione-sparing functions, anti-viral actions, anti-inflammatory capabilities, anti-neurodegenerative effects, and life-extending potency.[28-30] This last benefit – increased life span - is still a subject of debate, as the effects of resveratrol on lifespan have been observed only in non-mammalian organisms.[25] Still, studies have shown that resveratrol has beneficial effects on patients with a variety of cardiovascular and metabolic diseases, including type 2 diabetes.[31-32]

Dietary Sources

The benefits of resveratrol can be obtained from red wine, the skins of red grapes, purple grape juice, mulberries, and – to some extent – peanuts.

See the following table for details.

Dietary Sources of Resveratrol

Food/Beverage	Serving	Resveratrol (mg)
White wines (Spanish)	5 oz glass	0.01-0.27
Rosé wines (Spanish)	5-oz glass	0.06-0.53
Red wines (Spanish)	5-oz glass	0.29-1.89
Red wines (global)	5-oz glass	0.30-1.07
Red grape juice (Spanish)	5-oz glass	0.17-1.30
Peanuts (raw)	146 g	0.01-0.26
Peanuts (boiled)	180 g	0.32-1.28
Peanut butter	258 g	0.04-0.13
Red grapes	160 g	0.24-1.25

Source: Linus Pauling Institute (33)

Drug Interactions of Resveratrol

Resveratrol moderately interacts with medications that are changed or broken down by the liver. These include (but are not limited to) lovastatin, ketoconazole, itraconazole, fexofenadine, and triazolam. Resveratrol can slow down how quickly these medications are broken down, thereby increasing their effects and side effects.

Drugs designed to slow blood clotting (aspirin, ibuprofen, and diclofenac) also interact with resveratrol, since resveratrol slows blood clotting. Extremely slow blood clotting may result in bruising and excess bleeding.[34]

Conclusion

This chapter presented you with facts on three compounds with hypothesized antioxidant effects. There is some evidence that these compounds can be of benefit to type 2 diabetes patients, with lipoic acid showing the most promise. So if you are thinking about supplementing your diabetes treatment with alpha-lipoic acid, co-enzyme Q10, or resveratrol, talk to your doctor about a supplement plan appropriate to your condition.

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Vitamins and Diabetes

While a sound diet and regular exercise are crucial to lowering blood sugar, effective management of diabetes also involves adhering to the daily recommended vitamin intake. Would you like to reduce your incidence of infection and your number of diabetes-related sick days? In that case, getting in your daily vitamins is a good place to start.

One reason proper vitamin intake is so important is that diabetes causes your body to waste many important nutrients. Elevated glucose levels act like a diuretic, causing these nutrients to be flushed away in the urine. As a consequence, people with type 2 diabetes are likely to be deficient in important water-soluble vitamins and minerals.

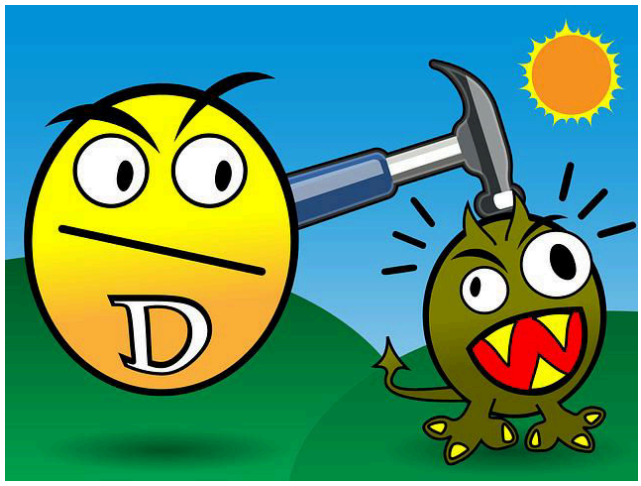
Furthermore, diabetes comes with a package of comorbidities and complications, such as cancer, fatty liver disease, and sleep apnea. Therefore, it's especially

important for you to get your recommended daily intake of vitamins, to help you get a handle on these complications.

But before you sprint over to your local drug store to stock up on supplements, some essential facts need to be pointed out. Fact number one: taking vitamins in excess of the recommended daily allowance without the consent of your doctor may be harmful, because the risks may outweigh the benefits. Fact number two: the most effective way to consume vitamins is via food. Fact number three: it is always advisable to consult with your doctor before embarking upon a regime of vitamins and supplements.

Vitamins are an increasingly popular treatment option for diabetes. Although vitamins aren't meant to replace your prescribed therapies, many studies have noted benefits of vitamins on chronic diseases such as diabetes. There is no firm evidence indicating that vitamins can reverse diabetes, but we do know that vitamins are an essential component of sound health.

Vitamin D



It's called the sunshine vitamin for a reason. Unlike most vitamin deficiencies, which are caused by a lack of the particular nutrient in our diet, vitamin D deficiency is linked to a lack of exposure to sunlight. Countless studies now link vitamin D

deficiency with significantly increased rates of cancer, heart disease, osteoporosis, multiple sclerosis, and many other health problems.

Vitamin D is essential to the growth and maintenance of sturdy bones. Without this vitamin, calcium - the body's primary mineral - cannot be properly absorbed. But did you know that vitamin D also regulates how our nerves and muscles work? And that it is useful in reducing internal inflammation - which in turn prevents chronic diseases, like heart disease and type 2 diabetes? Plus, countless preliminary reports have led researchers to conclude that vitamin D can prevent type 2 diabetes in high-risk individuals (i.e. people with pre-diabetes); however, more research is required to make a definitive conclusion.

Vitamin D is important because the beta cells of the pancreas need vitamin D to perform certain functions connected to glucose control.[1] It has also been noted that vitamin D sensitizes cells to the effects of insulin. This means that if you are a type 2 diabetic, vitamin D can help you combat the effects of insulin resistance.[2,3]

Three reviews from 2011, 2012, and 2013 found that individuals with increased levels of vitamin D displayed a decreased risk of developing type 2 diabetes! Think about that - just a 4 ng/ml increase in vitamin D can bring about a 4% reduced risk of developing type 2 diabetes in later life.[4] However, vitamin D is not a cure-all; after analyzing a series of studies on vitamin D, researchers reported that while vitamin D deficiency was common among patients with type 2 diabetes, they failed to find a link between vitamin D deficiency and insulin resistance.[5]

Although short-term vitamin D supplementation failed to produce any effects on blood sugar in individuals with pre-diabetes, there is ample evidence that it leads to improved insulin sensitivity in those who already have type 2 diabetes.[6,7]

More research is clearly needed before any definite conclusions can be made about the link between vitamin D with diabetes. However, we do know that people newly diagnosed with type 2 diabetes tend to have lower levels of vitamin D than those without the disease, as they tend to have poorer diets in general. For that reason alone, it is important to do everything in your power to attain balanced levels of vitamin D in your body.[8]

Dietary Sources

If you live in a Northern environment, where the long winters limit your exposure to the sun, you may be wondering how to boost your vitamin D levels. Normally, vitamin D is a fat-soluble vitamin present in only a limited number of foods. Fortunately though, vitamin D is

available as a dietary supplement, and it is also fortified in some foods. Milk, for example, always has added vitamin D. Orange juice, margarine, and soy beverage are usually enriched with it as well.

Children and adults (age 9+, including pregnant and lactating women) should get 600 IU of vitamin D per day, and should consume no more than 4000 IU per day. These daily allowances are based on minimal sun exposure.[9] Numerous studies note the positive effects of vitamin D when administered at modest doses of 1000 IU/day.[8]

Note that people with dark skin have a reduced ability to create vitamin D from sunlight and have a heightened susceptibility to vitamin D deficiency. People following a vegan diet have similar difficulties. Therefore, if you fall into either of these categories, make sure you're taking supplements.[9]

Food Sources of Vitamin D

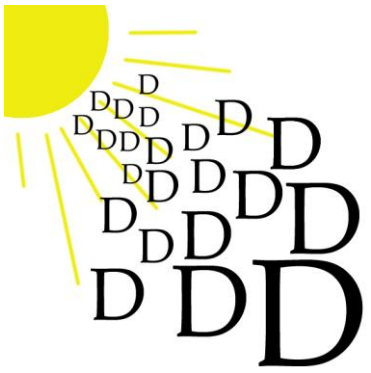
Food	Serving Size	Vitamin D (IU)
Cod Liver Oil	1 tbsp	1,360
Swordfish	2.5 oz (1 small filet)	471
Salmon, Sockeye (cooked)	2.5 oz (1 small filet)	372.5
Tuna (canned in water)	3 oz (half can)	154
Sardines (canned in oil)	2 sardines	46
Egg Yolk	1	41

Source: National Institutes of Health[9]

As we all know, too much of anything is bad for you. Although vitamin D toxicity cannot occur from exposure to sunlight or from vitamin D-containing foods,

supplements can cause non-specific symptoms such as anorexia, weight loss, and heart arrhythmias.[9] So make sure you discuss your desire to take vitamin D with your doctor before taking any supplements.

Absorption



Like all fat-soluble vitamins, vitamin D requires fat for it to be metabolized by your body. Luckily, all food sources of vitamin D contain fat. However, people who suffer from fat malabsorption (due to liver disease, celiac disease, Crohn's disease, etc.) should be aware that they may have a reduced ability to absorb vitamin D.[9]

Fat-soluble vitamins may compete against each other for absorption. This means that if you are already taking vitamin A, vitamin D may have difficulty being absorbed. Therefore, long-term consumption of excess vitamin A may lead to a vitamin D deficiency, potentially resulting in vitamin D-related health problems.[9]

Interactions Between Vitamin D and Other Substances

When it comes to health, your efforts to get the right balance can be easily undermined by the wrong prescription drug. That's why you need to exercise caution and vigilance with medications. Corticosteroid medications (such as prednisone), for

example, can reduce calcium absorption and impair vitamin D metabolism. Over the long term, the effects of corticosteroids can become worrisome.[10] So, be sure to discuss your vitamin D and calcium status with your physician if you need to take corticosteroids on a long-term basis.

Are you on trying to lose weight? If so, weight-loss drugs (which block fat absorption) and cholesterol-lowering drugs can reduce vitamin D absorption.[10] Therefore, it is important to consult with your doctor when taking these medications.

Finally, phenobarbital and phenytoin (for seizure prevention) increase the metabolism of vitamin D in the liver and reduce calcium absorption. Patients taking these medications may need to supplement their vitamin D and calcium intake.[11]

Vitamin B12

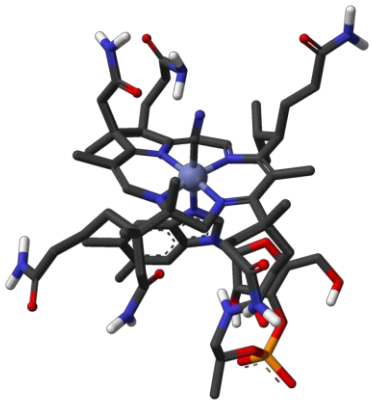
Of all the vitamins, B12 has one of the largest and most complex chemical structures. It is a water-soluble vitamin that is essential for your body to maintain normal function of the brain and nervous system. Vitamin B12 is also involved in DNA synthesis and cell growth.

Knowing the facts about the micronutrient vitamin B12 is of vital importance for a diabetic. Because diabetes puts you at risk of being vitamin B12-deficient, you

need to be aware of how this will affect your body, and of what you can do to boost your B12 levels to ensure optimal health.

If you're a diabetic taking metformin, you have an increased susceptibility to vitamin B12 deficiency. This deficiency is also common amongst patients with type 1 diabetes, due to a condition called pernicious anemia.[12]

You need to be especially vigilant about vitamin B12 deficiency, as it has been shown to worsen diabetic neuropathy. The good news is that vitamin B12 replacement has been shown to improve neuropathy symptoms such as pain and paresthesias.[12]



3D structure of vitamin B12

Given the risks, it's obvious that maximizing your B12 intake via your diet is a top priority if you're diabetic. Vitamin B12 can be stored long-term by the body, so it's the average daily consumption that counts. But keep in mind that if your physician diagnoses you with a severe vitamin B12 deficiency, supplementation may be required.[12]

Nutrition

The table below lists the daily recommended allowance for vitamin B12:

Recommended Daily Vitamin B12 Intake

Age	Recommended Daily Allowance (µg)
Children (9-13 years)	1.8
Adults (14+)	2.4
Pregnant Women	2.6
Lactating Women	2.8

Source: National Institutes of Health (13)

Don't worry about B12 toxicity if your doctor prescribes a supplement. There is no established tolerable upper limit for this vitamin. Clinical trials have demonstrated that vitamin B12 supplementation did not cause any serious side effects when administered at doses of 400 µg for 40 months.[13] So, go right ahead and talk to your doctor about whether a supplement is right for you.

Dietary Sources

The majority of vitamin B12 sources are animal-based. Therefore, vegetarians and vegans are at the highest risk of developing vitamin B12 deficiency. If you are a diabetic practicing a vegan or vegetarian diet, you need to ensure that you are

getting your vitamin B12 through fortified foods (e.g. breakfast cereals, nutritional yeast, soy products).[13]

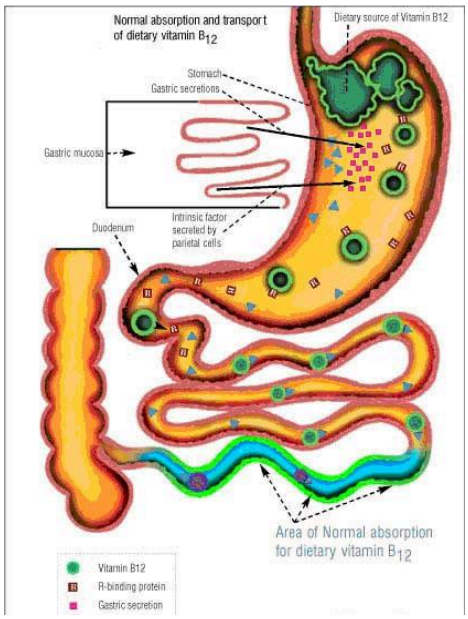
Food Sources of Vitamin B12

Food	Serving Size	Vitamin B12 (µg)
Clams	2.5 oz	70
Liver (Beef)	2.5 oz	59
Trout (Wild)	2.5 oz (small filet)	4.5
Salmon	2.5 oz (small filet)	4
Tuna	3 oz (half can)	2
Haddock	2.5 oz (small filet)	1.5
Beef	2.5 oz	1.7
Milk (Low-fat)	1 cup	1.2
Yogurt (Low-fat)	8 oz (small container)	1.1

Sources: US National Institutes of Health, Dieticians of Canada[13,14]

Absorption

Here's the kicker about supplements and why getting B12 from your diet is so important: our body has a limited ability to absorb vitamin B12 from supplements; approximately 10 µg of vitamin B12 is actually absorbed from a 500 µg oral supplement in healthy individuals.[13]



Furthermore, if you are an older diabetic or a diabetic suffering from pernicious anemia, reduced levels of stomach acidity (e.g. if you have hypochlorhydria or achlorhydria) or intestinal disorders may make it difficult to absorb vitamin B12 from food and oral supplements. Therefore, if you cannot absorb the vitamin through your gut, vitamin B12 can be given to you as an injection.

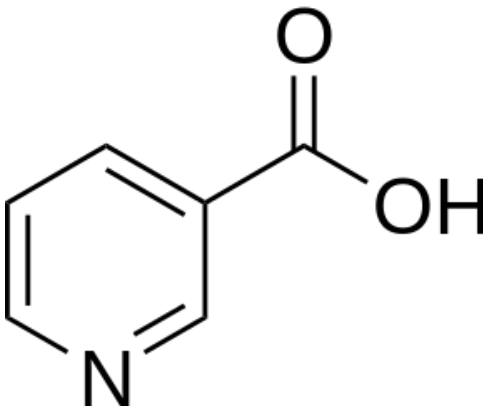
Interactions Between Vitamin B12 and Other Substances

The absorption of vitamin B12 can be affected by other medications. Proton pump inhibitors, such as omeprazole and lansoprazole (for gastroesophageal reflux disease or peptic ulcer disease), and histamine H2 receptor antagonists, such as cimetidine, famotidine, and ranitidine (for peptic ulcer disease) can interfere with vitamin B12 absorption in the stomach. So if you're taking these medications, make sure that you talk to your physician to ensure that you're metabolizing vitamin B12 properly.[13]

Metformin (for hyperglycemia and diabetes) is the most common type 2 diabetes medication and may also reduce vitamin B12 absorption. Therefore, you may need to consider a supplement of vitamin B12 if you're taking metformin.[13]

Vitamin B3

Vitamin B3, or niacin, is a fat buster. Specifically, it reduces fat content and increases good cholesterol. Niacin has been a well-accepted treatment for high cholesterol since the 1950s. Therefore, since cholesterol and triglycerides are commonly elevated in patients with diabetes, niacin may represent a potential therapy for these individuals. But before you go out to buy a supply of niacin, keep in mind that use of niacin as a treatment for type 2 diabetes is regarded as controversial. This is because it could have exacerbating effects on blood sugar control.



Chemical structure of niacin.

While the claims that niacin increases blood sugar are well substantiated, it is nevertheless, possible for diabetics to use niacin safely in conjunction with a doctor's supervision. A study of 468 participants, including 125 diabetics, found that 3000 mg/day of niacin for up to 60 weeks elicited significant increases in good cholesterol (HDL), and significant decreases in triglycerides and bad cholesterol (LDL) (15). It was observed that niacin only modestly increased glucose levels in diabetic and non-diabetic participants.[15] These results suggest that lipid-modifying dosages of niacin can be used safely in patients with diabetes.

The above results were corroborated by a 2008 review of all studies of niacin's effects on diabetic patients within the previous decade. The studies highlighted the clinical benefits of niacin treatment on incidence of cardiovascular events and

atherosclerosis, despite modest decreases in glucose control. In most cases, the benefits outweigh the risks. Even still, treatment guidelines recommend monitoring glycemic control after initiating niacin treatment or increasing its dosage.[16]

So discuss niacin with your doctor. Although there are risks, the doses of niacin that would be required to worsen your blood sugar control are very high - way higher than the niacin levels metabolized from food. You should therefore make sure that you are always getting adequate niacin in your diet, and only take supplements if directed by a physician.

Nutrition

Niacin is a water-soluble vitamin that isn't stored in the body.[17] It is typically prescribed in doses of 500 mg or more per day for managing cholesterol and triglyceride levels.[18]

Recommended Daily Niacin Intake

Age	Recommended Daily Allowance (mg)
Children (9-13 years)	12
Men (14+)	16
Women (14+)	14
Pregnant Women	18
Lactating Women	17

Source: National Institutes of Health[18]

The tolerable upper limit for niacin is 35 mg per day. Niacin is sometimes used in amounts exceeding the tolerable upper limit, in order to lower cholesterol levels. However, high doses of niacin can cause liver injury,[19] and niacin supplements exceeding the tolerable upper limit should only be taken if advised by a physician.

Dietary Sources

Yeast extract spread, think vegemite or marmite, has the highest measured amount of niacin. However, if these are not to your taste, you can refer to the table below to find other sources of this nutrient.

Food sources of Niacin (vitamin B3) include dairy, poultry, fish, lean meat, nuts and eggs

A.D.A.M.

Food Sources of Niacin

Food	Serving Size	Niacin (mg)
Yeast extract spread (marmite or vegemite)	2 tbsp	38
Anchovies	2.5 oz	19
Tuna	3 oz (half can)	14–22
Salmon	2.5 (small filet)	11–17
Liver (chicken, turkey, pork, beef)	2.5 oz	10–17
Chicken	2.5 oz	8–15
Rainbow Trout	2.5 (small filet)	8–10
Tempeh/fermented soy	¾ cup	8
Pumpkin, Squash Seeds	¼ cup	8

Source: Dieticians of Canada[17]

Absorption

Niacin is water-soluble and is rapidly absorbed in the stomach and in the upper part of the small intestine. It is observed 10 to 20 minutes in the plasma following absorption through the stomach, and when it is absorbed through the small intestine, it is observed 5 to 10 minutes later in the plasma.[20]

Cautions

Several precautions and warnings apply when taking niacin in doses exceeding the tolerable upper limit. Discuss these concerns with your physician before taking niacin supplements in high concentrations.[21]

Common side effects of niacin are flushing and a temporary increase in blood flow, which can cause burning, tingling, itching, redness in the face, arms, and chest, as well as headaches.[21]

Vitamin C

There is mounting evidence that vitamin C, as well as a high intake of vegetables and fruits, may have protective effects against diabetes. Plus, vitamin C lowers levels of sorbitol, a sugar that can collect in and damage cells in the eyes, kidneys, and nerves.

Diabetes is a disease linked to oxidative damage (damage done to your cells and DNA by rogue molecules called free radicals). Antioxidants, like vitamin C, can help protect against this damage; indeed, a study of over 21,000 men and women

found that higher blood vitamin C levels correlated with a reduced risk of developing type 2 diabetes.[22]

Equally impressive was the significant improvement in glycemic control observed in patients with type 2 diabetes, after they ingested 1000 mg/day of vitamin C for six weeks. However, no changes were observed in patients with type 2 diabetes who consumed only 500 mg/day of vitamin C.[23]

These results were corroborated by a recent study of type 2 diabetes patients who were taking metformin. The study noted that supplementation with vitamin C (1000 mg/day) for 12 weeks led to improved glycemic control.[24]

Finally, a 16-year-long study concluded that vitamin C supplementation of 400 mg/day or more was associated with significant reductions in coronary heart disease, a common complication of diabetes (26).

Thus, with very little effort, vitamin C can pay huge dividends when it comes to your health. Its antioxidant properties can help combat the progression of complications related to diabetes. So load up on the antioxidant goodness and make sure you're getting your daily dosage of vitamin C.

Nutrition

Vitamin C, also called ascorbic acid, is an essential water-soluble vitamin, which cannot be synthesized or stored by the human body. For this reason, vitamin C must be consumed every day, since excess or unused vitamin C is excreted into the urine via the kidneys.

The following chart contains the recommended daily intake and tolerable upper intake levels of vitamin C:

Vitamin C Recommended Daily Allowance

Age	Recommended Daily Allowance (mg)*	Tolerable Upper Intake Levels (mg)
Children (9-13 years)	45	1200
Teenage Boys (14–18)	75	1800
Men (19+)	90	2000
Teenage Girls (14–18)	65	1800
Women (19+)	75	2000
Pregnant Women	85	2000
Lactating Women	130	2000

Source: National Institutes of Health[27]

** Individuals who smoke cigarettes require 35 mg of additional vitamin C per day.*

Unlike niacin, vitamin C has low toxicity and has not been found to cause serious side effects. As indicated in the chart above, you need not worry about excess vitamin C, because you would have to consume an enormous amount of it before experiencing any immediate discomfort. Common complaints associated with high doses of vitamin C include diarrhea, nausea, and abdominal cramps, probably due to interference of the vitamin with other processes in the gastrointestinal tract .[27]

Still, there are conditions where you need to be conscious of how much vitamin C you are consuming. For example, a study of postmenopausal women correlated supplemental vitamin C uptake of more than 300 mg/day with an increase in

cardiovascular disease mortality.[27] Keep in mind that there is also some uncorroborated evidence suggesting that excess vitamin C consumption can lead to the development of kidney stones. Furthermore, a few studies have suggested that under certain conditions, vitamin C can act as a pro-oxidant (opposite of an anti-oxidant), causing damage to DNA and contributing to cancer. Since adequate vitamin C levels are easily consumed through diet, there should be no need to take vitamin C supplements, unless advised to do so by a physician.[27]

Dietary Sources

For many people, citrus fruits come to mind at the mention of vitamin C. But it's not just oranges and grapefruits that will allow you to reap the benefits of this nutrient. It can also be found in a wide variety of non-citrus fruits and vegetables. Unfortunately, vitamin C is not available in food sources that have been preserved for extended periods of time. So people who have limited access to fresh food on a long-term basis are more likely to suffer from a vitamin C deficiency.

Food sources of vitamin C

Food	Serving Size	Vitamin C (mg)
Red Pepper (raw)	½ cup	95
Orange Juice	¾ cup	93
Orange	1 medium	70
Grapefruit juice	¾ cup	70
Kiwifruit	1 medium	64
Green Pepper (raw)	½ cup	60
Broccoli (cooked)	½ cup	51
Strawberries	½ cup sliced	49
Brussels Sprouts (cooked)	½ cup	48
Tomato Juice	¾ cup	33
Cantaloupe	½ cup	29
Potato (baked)	1 medium	17
Tomato (raw)	1 medium	17

Source: US National Institutes of Health (27)

Absorption

Approximately 70%–90% of vitamin C is absorbed at moderate intakes of 30–180 mg/day. At doses above 1 g/day, absorption falls to less than 50%, while the unmetabolized ascorbic acid is excreted in the urine.[27] This is why it's futile to consume vitamin C in excess, as the body cannot utilize it.

In general, vitamin C is easily absorbed by most individuals. However, individuals with severe intestinal malabsorption conditions or end-stage renal disease may be at risk of vitamin C deficiency.[27]

Interactions Between Vitamin C and Other Substances

Vitamin C, when combined with other antioxidants, may affect the increase in high-density lipoprotein levels (good cholesterol) resulting from niacin–simvastatin combination therapy. However, it is not known whether this interaction occurs with other lipid-altering regimens. Healthcare providers should regularly monitor your lipid levels if you are taking both statins and antioxidant supplements.[27]

As mentioned previously, vitamin C is an antioxidant, which has been studied for its role in cancer prevention. However, the safety and efficacy of administering vitamin C (and other antioxidants) during chemotherapy is controversial. Some studies show that antioxidants may shield cancerous cells from the effects of chemotherapy, while others suggest that vitamin C may protect normal cells from the deleterious effects of chemotherapy. Individuals undergoing chemotherapy

should discuss their dietary and supplemental vitamin C intake with their oncologists.[27]

Vitamin E

Diabetes produces a state of increased free radical activity, which then damages tissues and cells.[28] However, studies suggest that vitamin E (an antioxidant) may protect your blood vessels and nerves from such damage.

Although the science is inconclusive, studies suggest that vitamin E improves glucose control, insulin sensitivity, and insulin secretion through unknown mechanisms.[28] A study of patients with type 1 diabetes reported decreases in blood glucose levels after 3 months of vitamin E supplementation, at a low dose of 100 IU/day.[30] A systematic review looking at the results of 6 studies also reported that in four of the studies, vitamin E improved glucose control (ranging from 100 to

1,600 mg/day for 2 to 4 months) in patients with type 2 diabetes. However, the largest of these studies found no change in blood glucose levels.[28] Furthermore, it has been shown that just 1,800 IU/day (for 4 months) of vitamin E treatment can elicit significant improvements in retinal blood flow and kidney function, though without affecting the average blood glucose-concentration.[29]

Finally, although there is insufficient evidence to determine whether vitamin E can control blood sugar levels in diabetic patients, there is data showing that the antioxidative effects of vitamin E can protect you against many of the co-morbidities associated with diabetes (e.g. retinopathy, neuropathy, and kidney disease). Therefore, don't shy away from vitamin E; it may yield some great benefits.

Nutrition

The upper limits for vitamin E intake are based on the risk of hemorrhagic stroke in patients taking vitamin E supplements; these limits are based on the results of two clinical trials.[31]

However, you need not worry about the adverse effects of consuming vitamin E as part of your diet, as you are unlikely to exceed the tolerable upper intake level by ingesting it solely through food.

The daily dietary targets for vitamin E in healthy individuals are listed in the chart below:

Recommended Daily Vitamin E Intake

Age	Recommended Daily Allowance (mg)	Tolerable Upper Intake Levels
Children (9-13 years)	11	600 mg (900 IU)
Teenagers (14–18)	15	800 mg (1200 IU)
Adults (19+)	15	1000 mg (1500 IU)
Lactating Women	19	1000 mg (1500 IU)

Source: National Institutes of Health[31]

Dietary Sources

Vitamin E is fat-soluble and is found in a number of different oils and nuts (among other things). Note that low-fat diets may provide insufficient amounts of vitamin E unless you select healthy fats and increase your intake of nuts, seeds, fruits, and vegetables (31). The foods richest in vitamin E are listed in the following chart.

Food Sources of Vitamin E

Food	Serving Size	Vitamin E (µg)
Wheat Germ Oil	1 tbsp	20.3
Sunflower Seeds	¼ cup (handful)	8–13
Spinach (boiled)	½ cup	10
Almonds (unblanched)	¼ cup (handful)	9–10
Broccoli (boiled)	½ cup	6
Kiwi	1 medium	6
Cereal, Wheat Germ	¼ cup	5
Peanuts	¼ cup (handful)	3
Oil (Sunflower, Safflower)	1 tsp	2

Source: US National Institutes of Health, Dieticians of Canada[31,32]

Absorption

To absorb vitamin E, the digestive tract requires fat. Bile acids are secreted by the liver into the small intestine, where they function to aid in the digestion of dietary fat.[31] Studies have found that vitamin E is absorbed only when consumed in a moderately high-fat meal (about 17 g of fat). Low-fat milk or low-fat breakfast cereal was found to be insufficient in promoting vitamin E absorption.[33]

Interactions Between Vitamin E and Other Substances

Studies show that vitamin E can increase the risk of bleeding in patients taking anticoagulants (such as warfarin).[31] Oncologists also advise against consuming antioxidant supplements such as vitamin E during chemotherapy, as they may reduce chemotherapy-induced oxidative damage to cancerous cells.[31]

Conclusion

A good diet can supply you with most of the vitamins and minerals you need. However, sticking to a healthy diet day after day can be a challenge, which is why many people rely on a daily multivitamin. While a supplement can't supply all of the essential elements found in fruits, vegetables, and whole grains, it can help to fill in some of the nutritional gaps in our diet.

Nutritional needs vary from person to person. Women who are pregnant or breastfeeding, people with particular diseases, the elderly, vegans, people on restricted diets or low-calorie diets, and people who do not eat a diet rich in fruits, vegetables, whole grains, low-fat meat, and dairy products, may need to resort to supplements.

If you have diabetes or pre-diabetes, then eating a healthy diet, trying to stay slim, doing regular aerobic exercise, and not smoking should be your mainstay in lowering your risk of future problems. However, vitamin supplementation may also provide some benefit; should you have any questions about whether you ought to be taking additional vitamins or minerals, speak to your healthcare provider.

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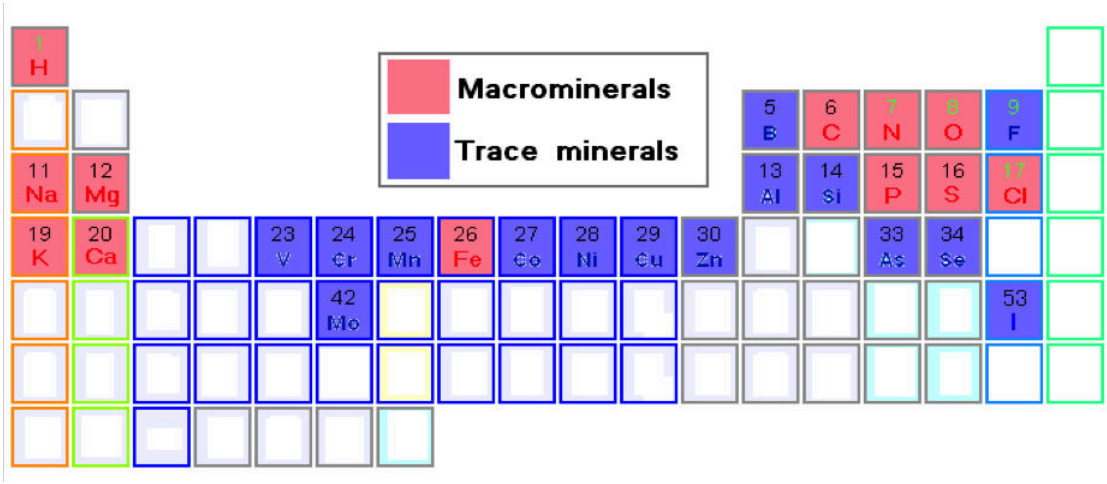
Minerals and Diabetes



Your body depends on minerals for a variety of different functions, including bone building, hormone production and maintenance of a regular heartbeat. There are two varieties of minerals: macrominerals and trace minerals. Your body requires larger amounts of macrominerals, which include phosphorous, calcium and sodium. Smaller amounts of trace minerals such as iron, copper and zinc are also needed by your body to ensure sound health.

Depending on the type of diabetes that you have been diagnosed with, and the treatment you follow, there are a number of minerals that may help with your condition. With that in mind, this chapter will look at some of the best mineral options available to you. Just remember, before rushing out and purchasing a supplement to add to your diabetes treatment, please discuss the addition of the mineral supplement with your health care provider.

Dietary modification and lifestyle changes are regarded as the primary intervention for treating diabetes and getting the upper hand on your condition. By

implementing positive dietary and lifestyle changes, diabetes patients may require less - and in rare cases, no - pharmaceutical medications to control their disease. Patients with type 1 diabetes, however, will always be dependent upon insulin. Nevertheless, with the proper controls, including supplements, they can drastically reduce the incidence of complications, including neuropathy and nephropathy.[1]

This chapter is focused on foods you should eat to increase your daily consumption of the minerals mentioned above. If you do decide to embrace a diet rich in minerals purported to improve diabetes, just ensure that such a change in your diet is compatible with your current diabetes treatment. Supplements are not substitutes for the medicine and recommendations provided by your physician, but are rather concomitant treatment options with the potential to help you achieve your medical goals.

The American Diabetic Association recommends that diabetics consume the same quantities of minerals as recommended for the general public, and does not advocate mineral supplements unless you are at an increased risk of deficiency. Therefore, talk to your doctor before taking mineral supplements. And even if your diabetes improves, don't stop taking your prescribed medication, unless your doctor says that it’s safe to do so.

Magnesium

Magnesium is an essential mineral and nutrient required by your body for various functions, including the regulation of muscle and nerve mechanisms, blood sugar levels, and blood pressure. Although a short-term deficiency in magnesium doesn’t

result in serious problems, long-term deficiencies can lead to a prolonged loss of appetite, nausea, vomiting, fatigue, and weakness.

Magnesium is the eleventh most abundant element in your body by mass, and is essential to the health and wellbeing of all your body's cells. Crucial for optimum health, magnesium helps to process proteins from food, serves as a building block for RNA and DNA syntheses and is a precursor for important neurotransmitters, such as serotonin.

Magnesium

Magnesium is absorbed in the intestines, and then excreted and reabsorbed in the kidneys to ensure appropriate levels of the mineral. People with chronic diseases such as gastrointestinal diseases or type 2 diabetes, which affect magnesium absorption or re-absorption in the kidneys, are at a heightened risk of developing deficiency in this mineral.[2]

Conversely, a meta-analysis of studies focusing on diabetes and magnesium consumption (via both food and supplements) between 1966 and 2007 found that individuals who consumed lower amounts of magnesium had a greater risk of developing diabetes.[3] The fact that magnesium helps to break down sugars is something you have to take note of. The exact mechanism of this breakdown in humans is unknown, but animal models have shown that a magnesium deficiency decreases the sensitivity of the insulin receptor, thereby decreasing the uptake of

glucose into the cells. Such a condition can lead to type 2 diabetes.[4] Magnesium also benefits control of high blood pressure, another common complication associated with type 2 diabetes.

However much of the evidence relating magnesium to glycemic control has been inconclusive. Some studies note a positive effect and others show no effect at all.[4,5] However, the latest research contends that restoring magnesium levels can improve insulin sensitivity and metabolic control in patients with type 2 diabetes, who are also taking the oral, diabetic medication, glibenclamide.[6] In another study – and this is especially important for diabetics – decreased insulin resistance was noted in patients taking magnesium supplementation.[7]

By ensuring adequate magnesium intake (particularly if you have been diagnosed as magnesium deficient) you can increase your glycemic control. Magnesium has also been found to be protective of blood vessels, thereby preventing damage commonly associated with both diabetes and chronic kidney diseases.[8]

Nutrition

Studies have concluded that the diets of many Americans are deficient in magnesium.[9] A mega analysis of nine studies, which administered 360 mg of magnesium per day to 370 patients with type 2 diabetes, found that magnesium supplementation reduced fasting blood glucose levels.[10] The recommended daily intakes of magnesium for healthy individuals are listed in the following table.

Recommended Daily Magnesium Intake

Age	Recommended Daily Allowance (mg)
Children (9-13 years)	240
Teenage Boys (14–19)	410
Teenage Girls (14–18)	360
Men (19–30)	400
Men (31+)	420
Women (19–30)	310
Women (31+)	320
Pregnant or Lactating Women	310–400

Source: National Institutes of Health[11]

[1] *The recommended daily allowance is the average daily level of intake sufficient to meet the nutrient requirement of nearly all healthy individuals.*[12]

[2] *The tolerable upper intake level is the maximum daily long-term nutrient consumption at which point individuals may experience adverse side effects.*[11]

The tolerable upper intake level of magnesium supplements is 350 mg a day, since the kidneys are unable to eliminate more than this amount through the urine. Too much of the mineral puts you at the risk of magnesium toxicity, which can result in impaired renal function, another common complication associated with diabetes.[11-13]

Therefore, never take magnesium supplements in excess of 350 mg per day unless under the direct supervision of a physician. High doses of magnesium can cause hypotension, nausea, vomiting, facial flushing, depression, lethargy and muscle weakness, difficulty breathing, irregular heartbeat, and cardiac arrest.[11]

Dietary Sources

Magnesium is widely found in fish and in plant foods, including leafy greens, nuts, legumes, and grains. The magnesium found in grains is usually contained within the germ and bran portion. This means that processed, non-whole-wheat breads contain very little magnesium. The following table summarizes the foods containing the highest amounts of magnesium:

Food Sources of Magnesium

Food	Serving size	Magnesium (mg)
Pumpkin/Squash Seeds	¼ cup	317
Brazil Nuts	¼ cup	133
Black-Eyed Peas	¾ cup	121
Sunflower Seed Butter	2 tbsp	120
Sunflower Seeds (Without Shell)	¼ cup	119
Tempeh/Fermented Soy	¾ cup	116
Soybeans (Cooked)	¾ cup	109
Soy Nuts	¼ cup	99
Almonds	¼ cup	88–109
Cereal (Bran)	1 oz	88–104
Wheat Germ Cereal	1 oz	96
Salmon	2.5 oz	92

Food Sources of Magnesium (Continued)

Food	Serving size	Magnesium (mg)
Beans (Cooked)	¾ cup	60–89
Cashews (Without Shell)	¼ cup	90
Halibut	2.5 oz	80
Spinach (Cooked)	½ cup	78
Mackerel	2.5 oz	73
Yeast Extract (Marmite/Vegemite)	2 tbsp	66
Pollock	2.5 oz	64
Lentils, Split Peas (Cooked)	¾ cup	52
Quinoa (Cooked)	½ cup	47

Sources: US National Institutes of Health, Dieticians of Canada[11,12]

Absorption

It is estimated that only 30–40% of dietary magnesium is actually absorbed by the body.[11,14] After entering the gastrointestinal tract through the mouth, magnesium is absorbed through the intestines, primarily the small intestine and potentially the colon. There are several strategies available for optimizing the amount of available magnesium that gets absorbed.

Spread magnesium consumption across several meals. The absorptive processes of the intestine and colon occur at a limited rate, which can become saturated; the percentage of magnesium absorption decreases with an increasing magnesium load.[15] This means that not all magnesium will have the chance to be absorbed if

consumed in excess within a small time frame. Therefore, consuming moderate amounts of magnesium with each meal will maximize its availability to the body.

Don't supplement with extreme doses of minerals. Minerals compete with one another in their quest to be transported through the intestines. Studies show that if you add excess amounts of calcium, phosphorus, magnesium, iron, copper or manganese, then the absorption of the other minerals will decrease as a consequence.[16]

Choose leavened wheat products. Phytic acid is a compound found in wheat, which binds minerals like magnesium and zinc, rendering them insoluble (unable to be absorbed). The process of making a loaf of bread or a cake rise during the baking process (known as leavening) requires yeast or baking powder, which breaks down phyticacid. While you don't necessarily need to avoid non-leavened wheat, you'll certainly get more bang for your buck if you chose leavened wheat products.[15]

Beware of Oxalates. Oxalates are found in plants, especially the leafy greens such as spinach, kale, Swiss chard, rhubarb and tea.[17] Studies on oxalates are inconclusive, but suggest that oxalates bind minerals like magnesium, and prevent their absorption by the body.[17] This is based on the observation that a higher proportion of magnesium was absorbed from kale than spinach (because kale contains fewer oxalates than spinach). But don't go swearing off spinach (a legitimate source of magnesium) – just apply the old adage of "everything in moderation" when it comes to leafy greens with oxalates.

For the best magnesium-boosting results, consume foods containing moderate-to-high amounts of magnesium on a regular basis. To experience the benefits of

magnesium, try to incorporate some of the foods listed above into your daily diet. And remember that long-term consumption of magnesium-rich foods are the safest, and probably most effective option.

Interactions Between Magnesium and Other Substances

Antibiotics and magnesium interact with each other in the body. Antibiotics are known to form chemical complexes with magnesium, reducing the availability of magnesium in the body. Not only does this phenomenon reduce the amount of magnesium, but it can also enhance the effects of antibiotics, which may not be desirable.[18] Antibiotics should be taken at least 2 hours before, or 4-6 hours after, a magnesium-containing supplement .[11]

Importantly diuretics increase the excretion of magnesium through the urine. To compensate for this, try to increase your magnesium consumption when taking diuretics.[19]

Chromium

Required by the human body in minute amounts, chromium is metallic element and an essential mineral for daily health. It is a key component of metabolic regulation and insulin delivery, and is also thought to be integral to carbohydrate, fat, and protein metabolism.[20] Chromium emerged as a potential treatment for type 2 diabetes over 40 years ago, and has been the second-most-popular mineral supplement in the US ever since.[5]

A deficiency in chromium is known to negatively affect glucose control, impairing the body's ability to use glucose, while forcing your body to increase its insulin requirements.[20] Recent studies have shown that the effect of chromium on glycemic control and insulin sensitivity is better observed in patients with glucose intolerance, insulin resistance, type 1 or type 2 diabetes, and gestational diabetes.[21]

Chromium

Although some of the data are inconclusive, there seems to be a possible effect of chromium on glycemic control. The disparity in results among different studies may be attributed to the fact that the type of chromium used tended to vary between studies.[5] Furthermore, it appears that those who stand to gain the most out of chromium supplementation are those who have an actual deficiency in the mineral.[20] This topic remains very controversial.

Chromium is thought to aid in glycemic control by enhancing the action of insulin. Data from a recent study suggests that chromium sensitizes cells to insulin by reducing the activity of the molecule regulating insulin receptors (a molecule that is also a pharmacological target for increasing insulin sensitivity in patients with type 2 diabetes).[22]

Nutrition

Chromium supplements are available in three forms. The doses used in clinical trials are as follows as chromium chloride (50–600 µg/day), chromium nitrate (200–800 µg /day), and chromium picolate (60–1000 µg /day). Studies show that chromium picolate is the most effective at treating diabetes.[5] The daily recommended allowances for chromium are listed in the following table:

Recommended Daily Chromium Intake

Age	Recommended Daily Allowance (mg)
Boys (9-13 years)	25
Girls (9-13 years)	21
Teenage Boys (14–19)	35
Teenage Girls (14–18)	24
Men (19–50)	35
Women (19–50)	25
Elderly Men (51+)	30
Elderly Women (51+)	20
Pregnant or Lactating Women	29–45

Source: National Institutes of Health

A nutritional deficiency in chromium is relatively rare in humans, but if you do have one, it can result in symptoms of type 2 diabetes that may be corrected via chromium replacements.[20] Few serious side effects have been linked to excess intakes of chromium. As a result, a tolerable upper intake limit has not been established for it .[20]

Dietary Sources

Chromium is found in a wide variety of foods, such as meats, grains, fruits, vegetables, and spices; however, most sources only provide small amounts, as few foods are 'rich' in chromium. The following table lists food sources of chromium.

Food Sources of Chromium

Food	Serving Size	Chromium(µg)
Broccoli	½ cup	11
Grape juice	1 cup	8
Red Wine	5 oz	1–13
English Muffin (Whole Wheat)	1	4
Bagel	1	3
Potatoes (Mashed)	1 cup	3
Garlic (Dried)	1 tsp	3
Turkey Breast	3 oz	2
Beef	3 oz	2
Orange Juice	8 oz	2
Basil (Dried)	1 tbsp	2

Sources: US National Institutes of Health (Chromium Page), Linus Pauling Institute

Absorption

Absorption of chromium from the intestinal tract is low, ranging from less than 0.4% to 2.5% of the amount consumed.[20] However, absorption of chromium is enhanced by vitamin C and niacin. After chromium is absorbed, it is stored in the liver, tissue, and bone.[20]

Chromium competes with iron for binding to a transport molecule necessary for absorption. Studies have shown that chromium supplementation does not impede iron absorption, though iron overload can interfere with chromium transport and absorption.[32]

An important diabetic note: consuming high amounts of simple sugars can lead to increased excretion of the body's chromium into the urine.[20] Therefore, if your blood sugar is high, you may need to replace chromium with supplements.

Toxicity of Chromium Picolinate

Chromium picolinate is the form of chromium that is most effective in glycemic control, though it may also have side effects.[5,23] Cellular experiments suggest that chromium picolinate may increase DNA damage (which could be potentially carcinogenic). However, researchers failed to replicate this finding in a study of 10 women taking 400 µg/day of chromium picolinate, which found no evidence of DNA damage.[23,24] Therefore, more studies are required to determine the safety of taking chromium picolinate at doses near 400 µg/day.

Many studies have demonstrated that doses of up to 1000 µg/day of chromium picolinate are also safe, though kidney failure has been associated with excess chromium ingestion.[23,25] Therefore, people with kidney conditions need be extra-cautious when taking chromium.

Always discuss the risks and benefits of chromium picolinate supplementation with a physician before starting any treatment.

Interactions Between Chromium and Other Substances

A number of medications (prescription and over-the-counter) can alter or impede the absorption and/or excretion of chromium. This means that individuals taking medications that decrease chromium absorption on a long-term basis may need to consider taking chromium supplements.

Antiacids, corticosteroids, H2 blockers (for gastroesophageal reflux disease) and proton pump inhibitors are medications that alter stomach acidity, and may also impair chromium absorption and enhance excretion through the feces.[20]

Chromium supplements can enhance the effects of a number of medications (prescription and over-the-counter), which in return may increase the absorption of chromium. Patients taking certain medications with chromium supplements need to be aware of these interactions and talk to their physician about the need to stagger doses. The effects of the following medications are potentially enhanced by chromium (20): beta-blockers, corticosteroids, insulin, nicotinic acid, nonsteroidal anti-inflammatory drugs (NSAIDS), prostaglandin inhibitors (ibuprofen, aspirin, etc.).

Vanadium

After medical science first hypothesized that this trace mineral could help control blood sugar levels by mimicking insulin, research studies on rodents and humans provided some encouraging results. However, to date, no one has been cured of their diabetes using vanadium supplements. In fact, many physicians have raised concerns over the potential damage caused by this mineral.

Vanadium

Vanadium is a trace mineral, found in very small amounts in a variety of foods. It is estimated that the average diet provides about 15–60 mg of vanadium per day.[5] However, its biological function is unclear, and no daily requirement has been established.[5] Though it is present in all your body's tissues, vanadium is not regarded as essential for survival.[26]

Clinical studies of vanadium and its effect on blood glucose regulation yield mixed results. Insulin-like properties of vanadium have been observed in experimental animal and cellular models; however, direct clinical evidence is lacking.[27] Several studies show small but significant benefits of vanadium supplementation on blood glucose levels.[28-33] However, the validity of these studies has been called into question owing to their small size, lack of control and failure to use rigorous methodologies.[27]

Unfortunately, vanadium has a poor therapeutic index, meaning that the dose required to demonstrate clinical efficacy is also likely to cause toxicity and/or side effects. The maximum tolerable limit for vanadium has been established as 1.8 mg/d,[5] though some clinical studies have administered vanadyl sulfate (an inorganic form of vanadium) in doses of up to 150 mg/day for several weeks. Currently, organic forms of vanadium are being proposed (in contrast to inorganic vanadyl sulfate), as they are more available to the body; in theory, this would reduce the dose required to produce effects, though there is no clinical data available on these new forms as of yet.

Side effects of vanadium supplementation are mostly gastro-related, and include nausea, vomiting, diarrhea, cramps, and gas.[5,26]

Dietary Sources

There have been no reports of vanadium toxicity from food consumption. Therefore, if you want to increase your vanadium intake, you could do so safely by consuming mushrooms, shellfish, black pepper, parsley, dill seeds, beer, wine, grain and grain products, foods that are considered as excellent sources of vanadium.[5]

Despite a dearth of clinical reports on the effects of vanadium deficiency, there are a number of reasons to add vanadium in your diet, including management of blood sugar, high cholesterol, heart disease, anemia and tuberculosis. If you are considering taking vanadium supplements, make sure to talk to your physician first.

Interactions Between Vanadium and Other Medications

Vanadium can interfere with the following medications[26]:

Anticoagulant or antiplatelet drugs
Vanadium can increase the risk of bleeding while taking these medications.

Drugs for diabetes
Vanadium supposedly decreases blood sugar; therefore, if you're already taking medications to control your blood sugar, then there could be a risk of your blood sugar levels becoming dangerously low.

Zinc

If you are concerned with improving your general health, then ensuring that you are getting enough zinc in your diet is crucial. Some scientists contend that even the smallest deficiency in zinc can have a terrible effect on your health because it is such a crucial mineral , directly related to cell division and hormone levels.

An essential trace element present in all organs, tissues, fluids and secretions of the body,[5] zinc also plays an important role in neural transmission in the brain.[34] Naturally available in food, it is crucial for immune function. Zinc deficiency can lead to infections, limit your sense of taste and smell, and result in difficulties seeing in the dark.[35]

Some studies have reported zinc deficiency with alterations in zinc metabolism in patients with diabetes.[5] A recent report showed that individuals with both type 1 and type 2 diabetes have significantly lower mean serum zinc levels compared with their healthy counterparts.[5]

There have been only a few studies on zinc supplementation and diabetes, and they yielded conflicting results.[5] Zinc supplementation of 30 mg/day for 12 weeks resulted in significantly decreased blood sugar levels.[5] However, another study demonstrated that zinc, magnesium, vitamin C, and vitamin E combination therapy were efficient at decreasing blood sugar levels; however, the study was unable to attribute these results to any of the micronutrients in isolation.[5]

This data suggests that both type 1 and type 2 diabetics have an increased susceptibility to developing a zinc deficiency. Although the link between zinc and blood sugar control is not entirely clear, we know that zinc is required for several bodily processes, and adequate levels must be consumed on a daily basis.

There are many factors that can alter the absorption of zinc, resulting in depleted storage of zinc in the body.[36] Therefore, zinc deficiency is a definite possibility, and can result from a combination of poor food choices and an imbalanced diet.

The recommended dietary zinc intakes for healthy individuals are listed in the chart below:

Recommended Daily Zinc Intake

Age	Recommended Daily Allowance (mg)	Tolerable Upper Intake Levels (mg)
Children (9-13 years)	8	23
Teenage Boys (14–18)	11	34
Teenage Girls (14–18)	9	34
Men (19+)	11	40
Women (19+)	8	40
Pregnant or Lactating Women	11–13	34–40

Source: National Institutes of Health[36]

The tolerable upper intake levels for zinc listed in the chart above do not apply to individuals receiving zinc for medical treatment if they are being monitored by a physician. Serious side effects leading to hospitalization are typically associated with daily zinc intake levels of greater than 80 mg per day; these effects include prostatic hyperplasia/urinary retention (benign prostatic hyperplasia), urinary tract infection, urinary lithiasis, and renal failure.[36,37]

Dietary Sources

Since zinc isn't stored by our bodies (unlike iron, for example), we must be sure to consume the required amount on a daily basis.[36] The best food source of zinc, by far, is oysters, with a whopping 137 mg per 2.5 oz serving (3–8 oysters). Other significant sources of zinc include lobster, crab, and other meats. Significant plant-based sources of zinc include certain nuts, seeds and legumes/beans.[36,38,39]

The foods listed in the following table are recommended for anyone looking to consume higher quantities of zinc in their diet:

Food Sources of Zinc for Meeting or Exceeding the Recommended Daily Allowance of Zinc.

Food	Serving Size	Zinc (mg)
Oysters	2.5 oz	25–137
Liver (Veal)	2.5 oz	8.4–8.9
Beef	2.5 oz	4.0–8.6
Baked Beans (Cooked)	¾ cup	4.3
Liver (Chicken, Beef, Lamb, Pork)	2.5 oz	3.0–6.0
Lobster	3.25 oz	2.9
Pumpkin/Squash Seeds	¼ cup	2.7–4.4
Veal	2.5 oz	2.3–7.4
Crab	2.5 oz	2.5–5.7

Sources: Dieticians of Canada, US National Institutes of Health[36,38]

Note that oysters, liver, beef, pork, and lamb are high-cholesterol foods that should be eaten in moderate amounts and should be avoided by people at risk of heart disease or stroke.

The foods listed in the following table provide are all sources of zinc, and will help you to reach the recommended allowance of 8–11 mg per day:

Food Sources of Zinc for Meeting the Recommended Daily Allowance of Zinc

Food	Serving size	Zinc (mg)
Tempeh/Fermented Soy	¾ cup	2.4
Wheat Germ	2 tbsp	2.4
Pork	2.5 oz (1 small filet)	2.3–3.9
Scallops	2.5 oz	2.3
Lamb	2.5 oz (1 small filet)	2.0–6.0
Mussels	2.5 oz (15 small or 8 large)	2.0
Chicken (Dark Meat)	2.5 oz (1 drumstick)	2.0
Lentils (Cooked)	¾ cup	1.9
Ricotta Cheese	½ cup	1.8
Cereal (Bran)	1 oz	1.7–2.2
Yogurt	8 oz (small container)	1.7
Eggs	2 large	1.3
Nuts	¼ cup (1 handful)	1.1–1.9

Sources: Dieticians of Canada, US National Institutes of Health[36,38]

Interactions Between Zinc and Other Substances

Antibiotics of the quinolone and tetracycline families inhibit the absorption of zinc. To avoid this type of interaction, it's best to consume zinc either 2 hours after or 4 hours prior to taking antibiotics. A similar phenomenon is observed with penicillamine (a drug used to treat rheumatoid arthritis); it's best to consume zinc 2 hours before taking penicillamine.[36]

Diuretics don't interact with zinc directly, but they work by increasing fluid excretion through the kidneys, causing zinc to be lost in the process. Long-term diuretic use could deplete zinc levels; therefore, this phenomenon requires monitoring by a physician.[40]

Phylates inhibit the absorption of zinc by the body. When consuming foods containing zinc plus phylates (such as whole grain breads, cereals, and legumes), the amount of zinc available to the body will be reduced.[36,41] For this reason, vegetarians may need to consume twice the amount of zinc as non-vegetarians; one strategy for increasing the amount of zinc available to your body involves soaking legumes, grains and seeds in water for several hours before cooking.[36]

Strategies for Maximizing Zinc Absorption by Body

Consuming zinc is the first step towards improved health. However, it must then be absorbed by the body. Taking the following measures will maximize the amount of zinc that your body absorbs:

Spread zinc consumption across several meals. Studies have found that relative zinc absorption is reduced with increasing concentrations of zinc in a meal, probably due to saturation of mineral transport mechanisms in the gut.[42] Consuming moderate amounts of zinc at every meal, instead of consuming high amounts in one meal, will likely lead to greater mineral absorption.

Avoid overloading on iron. Iron overload has potentially negative health consequences, but iron and zinc may also compete for uptake by the body via mechanisms that are not completely understood. Some studies support this hypothesis, while others refute it. In any case, moderate iron consumption has been shown to have no negative effect on zinc absorption.[42]

Consume zinc with high protein meals. Zinc absorption is likely to be greater when there is more protein in a meal. Luckily, most foods that are high in zinc are also high in protein.[42]

Increase your calcium intake. As mentioned previously, zinc absorption is inhibited by phylates. However, it is postulated that calcium may bind phylates, freeing up zinc in the process.[42]

Conclusion

In isolation, minerals cannot cure diabetes. However, patients with diabetes should ensure that they are getting adequate levels of minerals in their diet in order to prevent further complications and health problems. But in the end there is no cutting corners if you want to improve your health. Mineral supplements alone are

not magic pills that will cure you; yet if you remain vigilant and stick with a healthy game plan, your chances of winning the fight over diabetes will be radically improved.

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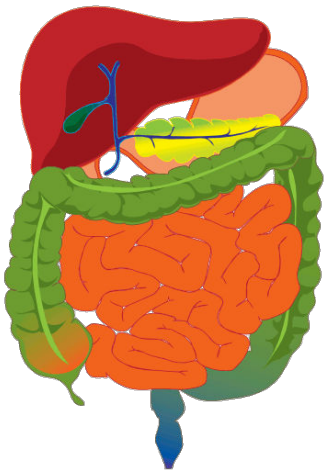
Probiotics and Diabetes

Probiotics have been marketed zealously by the food industry since the 1990s, when science turned its discerning eye towards the tiny microbes now hailed by the media as modern-day miracle workers. Probiotics are yeasts and live bacteria, which, once consumed, promote better health and an improved digestive system, by helping to keep your gut clean. Found in everything from yogurt to chocolate, probiotics are the subject of rising interest. Although many of their positive effects remain unproven, scientists continue to investigate their properties.

When probiotics (also known as 'good bacteria') are consumed, they join a community of organisms inside your intestines, consisting of bacteria (good and bad) and other microorganisms. This community is referred to as the gut flora. Some 100 trillion microorganisms make up the gut flora – that's ten times the number of cells in the human body.[1] Even though you can survive without it, the gut flora plays such an important role that some experts



have come to regard it as another organ within the body. Indeed, the microorganisms in the intestine contribute to an astonishing range of activities, such as immune system training, gut development regulation, vitamin production, and the inhibition of harmful bacteria.

Importantly, the term 'probiotic' doesn't refer to any one particular entity, but includes dozens of different strains of bacteria. Two of the most common groups of probiotics are *Lactobacillus* and *Bifidobacterium*.[1] Different strains can have different effects. Therefore, if one strain is found to aid management of a disease (e.g. diabetes), other strains may not necessarily have these benefits.[1] Keep this in mind when you read about probiotics. Do not be lured blindly by flashy advertisements for "probiotic" foods or drinks; the exact nature of the probiotic can vary, and different probiotics can have different effects on your health. However, this does not mean that these foods and drinks are ineffective; it just means you should use critical investigation tools to decide which probiotic will work best for you.

Two important factors to consider when characterizing each probiotic are strain and concentration.[1] Because there are so many different strains and concentrations that are beneficial to your digestive health, you should consider a mix of different probiotics, to help maximize your results.

Remember that when it comes to diabetes, probiotic research is still in its infancy. Right now, we do not know the extent to which probiotics will actually benefit your health. The purpose of the following section is to provide you with conclusions gathered from a number of different studies, which we hope will help you to make informed decisions about probiotics.

Clinical Trials

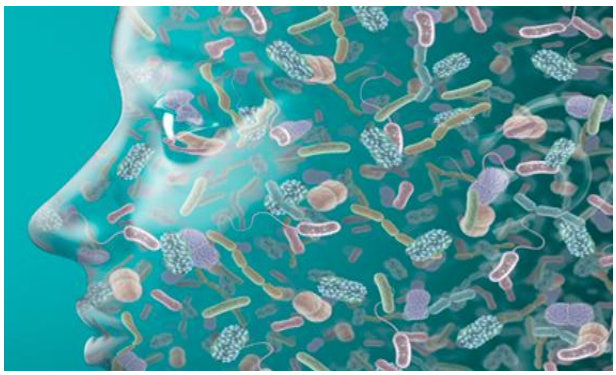
Anti-Diabetic Effects of Probiotics

There are a number of human studies that have looked into the anti-diabetic effects of probiotics, including two double-blind, randomized clinical trials. In both of these studies, type 2 diabetes patients were divided into two groups. One of these groups was given 300 g/day of probiotic yoghurt containing 106 cfu/ml *Lactobacillus acidophilus* La5 and 106 cfu/ml *Bifidobacterium lactis* Bb12 (cfu = colony forming units). The other was a control group consuming 300 g/day of conventional yoghurt.

The group taking the probiotic yogurt showed a significant decrease in fasting blood glucose levels and glycocylated haemoglobin (HbA1c), with a significant increase in antioxidant status.[3] A similar study in 60 patients showed a significant decrease in the proportion of low-density lipoprotein or LDL (known as 'bad cholesterol'). Their total cholesterol also decreased.[4] These results suggest that

probiotic yoghurt of this particular composition can reduce antihyperglycemia (high blood sugar) and can improve a person's lipid profile.[3,4]

A slightly different treatment - a drink consisting of 108 cfu/ml *L.acidophilus* and 108 cfu/ml *Bifidobacterium bifidum*–yielded similar results in elderly patients, over a duration of 30 days. HDL increased significantly, while cholesterol was reduced non-significantly. Also, blood sugar levels went down markedly.[5]



Positive, albeit more indirect results, have also been seen in pregnant women taking probiotics. One study measured levels of adiponectin in breast milk following birth. Higher adiponectin levels indicated a reduced chance of gestational diabetes. The probiotic treatment consisted of *Lactobacillus rhamnosus* combined with *B.lactis*, and it was found to significantly reduce the chances of gestational diabetes.[6,7]

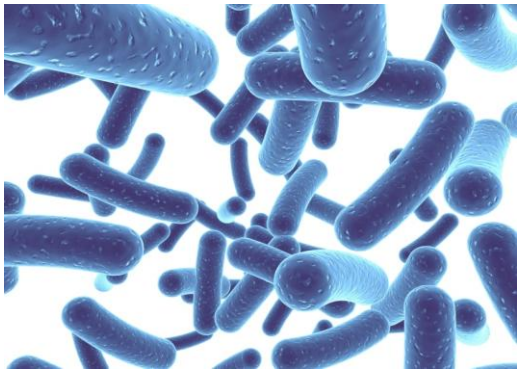
Similar improvements were observed in another double-blind, randomized clinical trial on pregnant women. Women who took *L.rhamnosus* and *B.lactis* until the end of exclusive breastfeeding experienced enhanced blood sugar control versus women who weren't taking probiotics. These beneficial effects extended over the 12-month postpartum period.[8]

An exciting discovery was made in early February 2015 concerning the use of a probiotic pill to treat type 1 and type 2 diabetes. Although probiotic pill research is still in its infancy, this study showed that the probiotic pill-induced cells of the gut

can produce insulin. However, these results have yet to be validated in humans. Even so, the implications are tremendous; if such a pill could be made safe and effective, patients with type 2 diabetes might be able to counter the glucose resistance that builds up in their bodies. For type 1 diabetics, the additional challenge of tackling the immune system would need to be considered in developing this pill.[9]

Contradictory Data on Anti-Diabetic Effects of Probiotics

The evidence in favor of probiotics is not unequivocal. In 2010, a double-blind, randomized study found that a specific commercial *L.acidophilus* product didn't improve diabetes measures in a group of men after four weeks.[6] However, it has been suggested that this may have occurred because the probiotic treatment wasn't tailored to the genetics of the subjects.[2]



Conclusion

A 2013 review of probiotics trials in diabetes patients concluded that "the purported anti-diabetic effects of probiotics have not been adequately validated in the target human population".[2] Based on the evidence we have presented, this is a reasonable take-home message. The results of probiotics research are varied, though an appreciable number of studies do suggest that probiotics may hold some

benefit for diabetics. However, further research is required both to replicate these studies' results, and to understand the precise conditions required to produce them. For now, consuming a diet incorporating moderate amounts of probiotic yoghurt intake may be beneficial, always keeping in mind that "probiotic" can refer to any of a variety of bacterial strains of different concentrations.

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Artificial Sweeteners and Diabetes

Are you trying to decrease the amount of sugar and the number of calories you consume? Perhaps part of your action plan involves replacing sugar with artificial sweeteners or some other type of sugar substitute. Well, as you'll come to see, the world of artificial sweeteners and sugar substitutes is vast and varied, and there are countless foods and beverages marketed as "sugar-free" or "diet." These include everything from soft drinks to baked goods and chewing gum. The exact nature of these sweeteners, and of the effect they have upon your diet and health, are going to be addressed in this chapter.

If you are overweight, or are dealing with diabetes, artificial sweeteners can provide you with an opportunity to indulge your sweet cravings without feeling guilty. As a diabetic, the positive aspect of artificial sweeteners is especially obvious: these additives give you the sweet taste of sugar without increasing your blood glucose levels.

However – and this is a very important point – substituting sugar for artificial sweeteners is not going to be enough to solve your blood sugar issues. It is not just sugar intake that diabetics need to control – you also need to balance your intake of fats. This will allow you to maintain a well-balanced diet, helping to keep your blood glucose levels under control.

Here are some facts about sugar substitutes that you might find interesting:

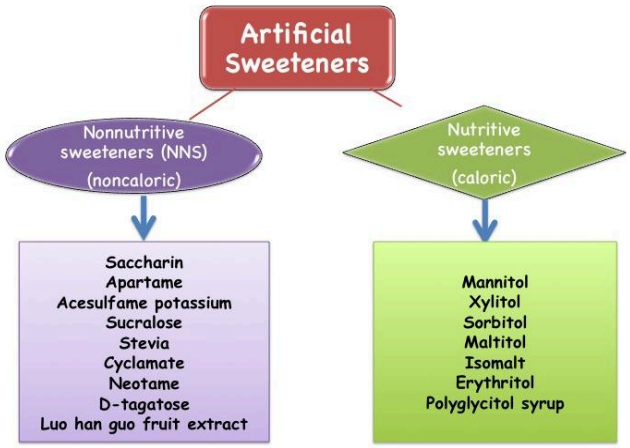
- A gram of artificial sugar is sweeter in intensity than other caloric sugar derivatives, such as corn syrup, honey, agave syrup or sucrose.

- There are two types of artificial sweeteners. One is known as a noncaloric or nonnutrient sweetener (NNS), since it does not increase your calorie count when consume.[1,2] Such sweeteners provide 30 to 13 000 times the sweetness of sucrose. Some examples of NNS are saccharin, Stevia, aspartame, acesulfame potassium, D-tagatose, and neotame. The second type of artificial sweetener, reduced caloric sweeteners, include sugar alcohols (polyols). Examples of sugar alcohols are lactitol, sorbitol, maltitol, erythritol, mannitol, tagatose, xylitol, and isomalt.[3] Reduced caloric sweeteners have approximately the same sweetness intensity as sucrose, and contribute some caloric intake when consumed.[4]

The acceptable dietary intake (ADI) per day for each of the above sweeteners has been formulated by the US Food and Drug Administration.[5] The ADI is the safe amount that can be eaten without any health risk to you over the course of your life. The actual ADI values for artificial sweeteners will be discussed in the following section.

Types of artificial sweeteners

You can find artificial sweeteners in many different kinds of products, including juice, yogurt, gum, and desserts. Normally, either the sweetener alone or a combination of the sweetener with sugar is added to the product.



Nonnutritive (NNS) or noncaloric sweeteners

An interesting fact about sweeteners is that many were accidentally discovered in laboratories. For example, the sweetener marketed under the brand name Splenda was discovered when a grad student misunderstood his professor's written instructions. He read "testing" as "tasting," and when he obligingly sampled one of the chemicals, he noted its sweet flavor.

This accident led to the development of a natural sugar supplement, which reduced caloric intake. Such nonnutritive, or noncaloric, sweeteners do not contain carbohydrates and provide minimal-to-no energy. Nonnutritive sweeteners are also known by a number of other names, like ‘low-calorie sweeteners’, or ‘intense sweeteners.’

Eight artificial nonnutritive sweeteners have been approved by the Food and Drug Administration (FDA) in the US and labeled as food additives: aspartame, saccharin, neotame, acesulfame potassium, Luo Han Guo fruit extract, D-tagatose, cyclamate, and sucralose. Diabetic individuals can make use of these artificial sweeteners, as they do not increase blood glucose levels and are not absorbed by the body. This reduced absorption ensures a decrease in your body’s calorie intake.[1,3]

The FDA regulates NNS as food additives. The approval process involves identifyingthe quantity of intake, understanding the combined effect of the compound based on its different uses, and the toxicology results based on studies with animals.

Nonnutritive sweeteners are used in a variety of different foods, such as cereals, beverages, and packaged foods. In the US, adults obtain 14.6% of their energy from nonnutritive sweeteners.[5]

In the US, nearly 85% of the population consumes food that contains NNS, while the small proportion of the population that does not consume NNS-foods generally avoids them because of perceived health risks.[6]

Part of the reason why there is a reduced risk of type 2 diabetes, cardiovascular disease, obesity, and prediabetes when using NNS is that individuals who incorporate NNS into their diet tend to consume more fruits and vegetables, to be careful about their diet, and to stay away from processed meat, sugars, and fatty foods.[6]

The following is a comprehensive list of the most common, FDA-approved artificial sweeteners for use by diabetics, pregnant women and children. All these sweeteners are regarded as safe when consumed within the ADI values. They are also the most common and readily available products on the North American market.

Stevia sweeteners (ie, Krisda, Stevia, Pure Via, Truvia)

These natural sweeteners have been approved for use in items like cereals, food spreads, gum, snacks, baked goods, and as table top sweeteners.[7]

Stevia is a natural plant product that is isolated from Stevia Rebaudiana; it is 100 to 150 times sweeter than sucrose.[8] The acceptable dietary intake of Stevia sweeteners for a day is 4 mg/kg of body weight. When baking, you can substitute a cup of sugar with 24 packets of Stevia.[9] Although Stevia has been provisionally approved by the FDA, it is not recommended for pregnant women.

Aspartame (eg, NutraSweet®, Equal®)

A sweetener that is 180 times sweeter than sugar,[8] aspartame was accidentally discovered in 1965 by James Schlatter. He discovered the sweetness of aspartame while developing a treatment for ulcers. Before turning the page of a book, he licked his finger and experienced a sweet taste on his fingertips due to the chemicals he had worked with. Aspartame has become a popular sweetener, since it replicates sugar's taste and can be metabolized easily.

Manufactured in tablet or in granulated form, aspartame is frequently found in chewing gum, beverages, dessert packages, cereal, vitamins, medications (sugar-free cough drops), gelatin, and yogurt. The ADI of aspartame for a day is 40 mg/kg body weight.[7]

Keep in mind that the flavor of aspartame may change when heated.[7] According to the manufacturer's recommendations, aspartame should not be used in high-temperature cooking, such as baking. Instead, it can be used as a sweetener in yogurts and drinks. Aspartame can be safely usedby pregnant women. However, these individuals should avoid consuming aspartame, as the fetus is unable to break it down.[10]

Saccharin (e.g. Sweet'N Low, Hermesetas)

This artificial sweetener was another accident, discovered by chemist Constantin Fahlberg while working in a laboratory at Johns Hopkins University in 1879 (11). When Fahlberg returned home after a day in the lab and sat down to a meal, his bread tasted unusually sweet; he quickly realized it was because of a chemical compound on his hands.

Saccharin is about 300 to 500 times sweeter than sugar.[8] It is frequently used to sweeten baked goods, jams, soft drinks, gum, vitamins, toothpaste, lip gloss, salad dressings, and mouthwash - to name just a few of the many products it can be found in. The ADI of saccharin per day is 5 mg for every kg of body weight.[7]

The manufacturer's recommendations provide the exact dose of saccharin that can be used in place of sugar. The general recommendations are to use either 2 tablespoons of saccharin liquid, 1 cup of brown sugar saccharin, or 24 packets of saccharin while baking, instead of 1 cup of sugar.[9] Saccharin can be safely used by pregnant women.[7]

Acesulfame potassium (e.g., Sunett®, Sweet One)

Discovered in 1967, the sweetness quotient of acesulfame potassium is 200 times that of sucrose; it is used as a tabletop sweetener and is also a common ingredient in frozen desserts, candies, beverages and medications, such as cough drops.[8] It is frequently used to help reduce and mask the bitter aftertaste of aspartame. The ADI

of acesulfame potassium per day is 15 mg for every kg of body weight (7). The manufacturer recommends replacing ¼ cup of sugar with 6 packets of Sweet One (15). Acesulfame potassium can also be safely consumed by pregnant women (7).

Sucralose (e.g., Splenda®)

This product was accidentally discovered in 1976 in London, while a group of scientists were attempting to create a new pesticide. Sucralose is 600 times sweeter than sugar.[8] The ADI of sucralose for per day is 9 mg for every kg of body weight.[7] It is used as a sweetener in all types of food and beverages: frozen desserts, gelatin, chewing gum, and fruit juice. For baking, one can replace one cup of sugar with a half cup of sucralose.[9] Sucralose is also safe to be used by pregnant women.[7]

Cyclamate (Sugar Twin®, Sucaryl®)

The sweetness of cyclamate is 30 to 50 times that of sugar and it is available in tablets and granulated form. The recommend ADI of cyclamate per day is 11 mg for every kg of body weight. Cyclamate was banned in the US from being added to food after studies showed its carcinogenic potential in animals. Hence, it is only used as a tabletop sweetener.[5]

Neotame

This is an artificial sweetener that is 7000 to 13 000 times sweeter than sugar. Neotame is now used in baked goods, gelatin, frozen desserts, jams, jellies, etc. Neotame contributes to a reduction in body weight and reduced weight gain.[10]

D-tagatose

This artificial sweetener has been assigned the Generally Recognized As Safe (GRAS) title by the FDA in the US. Other countries, like Canada, have still not recognized it as a safe-to-use sweetener in foods. However, D-tagatose can be found in ice creams, cakes, frosting, cheese, and yogurt. It has 92% of the sweetness of sucrose.[8]

Luo Han Guo fruit extract (Nectresse)

This is a fruit from the Siraitia grosvenori plant, and its extract is used in Chinese teas designed to treat coughs and sore throats. It is also useful in stimulating the bowels, and it is about 300 times sweeter than sugar.[12] Based on the manufacturer's recommendations, you can substitute 1 teaspoon of granular sugar with ¼ teaspoon of Nectresse.

Caloric sweeteners or nutritive sweeteners

Perceived sweetness has long played an important role when it comes to our enjoyment of various foods and beverages. Research indicates that humans enjoy sweet tastes more than any other taste sensation.

Caloric sweeteners include sucrose (table sugar), honey, molasses, agave, and high fructose corn syrup (HFCS), as well as simple sugars like glucose and fructose (fruit sugar) and complex sugars like lactose (milk sugar). Like most carbohydrates, caloric sweeteners provide 4 calories (17 kilojoules) per gram.

Nutritive sweeteners, or caloric sweeteners, contain carbohydrates and provide energy. They are sugar alcohols, also known as polyols, and are hydrogenated carbohydrates that can be used to replace sugar. Sugar polyols are found in small quantities in fruits and vegetables, such as plums, berries, and apples.[13]

Examples of polyolsinclude lactitol, sorbitol, maltitol, erythritol, mannitol, tagatose, xylitol, and isomalt. Polyols influence the glycemic index of foods, lowering their GIs. Other terms for polyols are ‘sugar replacer’ and ‘hydrogenated carbohydrate.’ It is important to remember that polyols are not sugars and can hence be added in sugar-free products, such as chocolate and toothpaste.[14] Although polyols are similar in structure to sugars, the former contains an alcohol molecule, while sugars contain a carbonyl molecule.

Polyols are less sweet than sugars but provide fewer calories, and this makes them an attractive alternative to sugar among weight-watchers and diabetics. Although polyols are found naturally, those used for commercial purposes are synthesized

from sugars.[13] These sugar polyols have been approved by the FDA and are classified under the category of caloric sweeteners or nutritive sweeteners.

Some of the beneficial characteristics of polyols are their low glycemic index (does not increase the blood glucose levels), their superior absorption in the colon, low cacrinogenicity (does not affect dental cavities), improved tolerance in the intestine, and low insulinaemia. This is due to the fact that polyols are not easily digested and metabolized, but are easily fermented in the colon.[14]

Since they are digested slowly and minimally absorbed by the stomach, there is limited release of glucose. Polyolsin the mouth are resistant to acidogenesis and fermentation by microorganisms that are present in the plaque of the teeth. Recent data has shown that xylitol is effective in reducing and reversing the process of dental decay.[15] Polyols that are not absorbed by the stomach are fermented in the colon. Thus, there is no dramatic increase in blood glucose levels.

Polydextrose is another type of nutritive sweetener, which is synthesized from dextrose (a form of glucose). Polydextrose is not sweet but provides a tart texture to many food products, such as puddings, desserts, candies, or cakes.

Depending on the quantity of polydextrose consumed, some individuals may experience gastrointestinal issues. Diabetic patients suffering from constipation may find relief after consuming polyols.[13]

Polyols have been approved as safe sugar substitutes for diabetic individuals as well as for weight watchers. However, individuals must consult with their health practitioner or family physician about the advantages of incorporating polyols into

their diet. But keep in mind that some of the negative effects associated with excess consumption of polyols are diarrhea and gastrointestinal problems.[13]

A couple of studies have noted that the polyol pathway may be responsible for the development of diabetic cataract. Aldose reductase is an enzyme, which converts glucose to sorbitol. Increased levels of sorbitol result in an increase in osmotic stress in the eyes, leading to swelling and eventual rupture. Diabetic cataract is commonly observed in both type 1 and type 2 patients.[17,18]

Effect of NNS Sweeteners on Diabetes Management

According to data from the Mcgill University Nutrition and Food Science Centre, it has been observed that nonnutrient sweeteners (such as sucralose, saccharin, aspartame, cyclamate, and D-tagatose) do not have any impact on the blood lipid and blood glucose levels of diabetic patients when consumed well below the permitted ADI limits. These results were based on daily consumption of these artificial sweeteners.[8]

Inconclusive data

In vivo human studies have discovered no adverse effects of nonnutrient sweeteners on blood glucose levels, insulin levels, appetite, or blood pressure.[19] However, data from animal studies, as well as from human epidemiological studies, indicate possible carcinogenic effects from aspartame. In Europe, the European Commission has requested that the European Food and Safety Authority

reassess the experimental data on aspartame in order to better understand its carcinogenic effects.[20]

Side Effects of Artificial Sweeteners

According to current data, the side effects of artificial sweeteners may include headaches, pre-term delivery, low birth weight, and even increased cancer risk.[4,21-23]

Carcinogenic Effects

Despite the data from animal studies showing carcinogenic effects of artificial sweeteners, these results have not been reproduced in human studies. A number of large sample studies have analyzed the association between low or no-calorie artificial sweeteners and cancer, and have observed that long-term use of sweeteners has no effect upon cancer.[23] Yet this did not stop saccharin from being withdrawn from the market in the US and Canada.

In 1991, the US finally withdrew the ban and saccharin is now added to foods. Even still, saccharin comes with a warning stating that it has the potential to cause cancer. Aspartame has also been shown to have carcinogenic potential in animal studies; it is also potentially harmful to pregnant women.[4]

Migraines

It has been noted that aspartame-containing products can induce migraines in certain individuals. Similarly, sucralose has the potential to cause migraines. Fortunately, these migraines dissipate when sucralose consumption is avoided.[4]

NNS sweeteners and obesity

In an attempt to identify the effect of NNS upon diet, a researcher named France Bellisle, from Quebec, Canada, has demonstrated that sweet-tasting food induces individuals to consume larger quantities. The effect of NNS on the number of calories consumed by the body varies according to the type of food. Thus, there is a difference between yogurt and chocolate in terms of the calories being ingested. The calorie intake is much higher in NNS-chocolate.

Food satiety (the feeling of fullness) is dependent on the calories consumed rather than the sweetness of the product itself. Therefore, fewer calories are ingested in NNS-foods than in foods containing added sugars. The result is that appetite is lower in individuals who consume NNS-rich foods.

It was found that individuals who consume NNS-rich food tend not to smoke, and also exercise regularly. It was also noted that individuals who regularly consume diet soft drinks tend to be more health conscious and make better dietary choices.[5,25] However, another study observed that diet soda causes an increase in fat around the gut area in individuals over the age of 65, increasing their risk of cardiovascular disease.[26]

It remains unclear whether artificially sweetened beverages have a negative effect on obesity. Although some data suggest that obesity may be complicated by artificially sweetened beverages, additional data is required to determine the exact influence of artificially sweetened beverages on individuals with diabetes, cardiovascular disease, and those trying to lose weight.[27-29] This is because numerous other studies have concluded that artificial sweeteners can actually help manage the weight of diabetic and obese individuals.[8]

NNS Sweeteners and Pregnancy

Studies have observed that regular consumption of NNS sweeteners by pregnant women can give rise to metabolic conditions such as hypertension, insulin resistance, and obesity in children. The suggested mechanisms stem from oxidative stress, an irregular appetite, enhanced absorption of glucose into the intestine, and changes in the microbiota of the intestine. Additional research is required to confirm the effects of NNS in pregnant women.[30]

Other studies have shown that sucralose, acesulfame-K, and aspartame can be used safely by pregnant women. Saccharin, however, is not to be used during gestation.[8] It was found to cause anemia, folate, vitamin A, and iron deficiency.[4]

Appetite

Appetite was found to be reduced when artificial sweeteners were consumed; neotame, for example, actually caused a drop in weight gain.[4]

Consumer-Packaged Foods

It is not necessary for the manufacturers of packaged foods to indicate the different forms of sugars (natural and artificial) that make up the total sugar content in the product. Furthermore, rounding rules are implemented in labeling nutrient guidelines on packaged foods. These rules (established by the FDA) maintain that if a packaged food contains less than 0.5 grams of sugar, the food is considered sugar free.

There is now an increasing tendency to purchase products with non-caloric sweeteners. In the US food market, 75% of packaged foods contain 73.5% caloric sweeteners and 1.5% non-caloric sweeteners. Without the exact sugar details, it is difficult to select products that specifically contain non-caloric sweeteners. It has been predicted that if details were provided regarding the sugars added to packaged products, food manufacturers would actually reduce the amount of sugars added to products, because of the increased transparency.

Conclusion

Artificial sweeteners are increasingly common sugar substitutes, found in countless packaged foods and drinks. If you have a sweet tooth and are concerned about the effect of your weight on your diabetes, perhaps sugar substitutes are a suitable alternative. However, keep in mind that in excess, some of these sweeteners may pose health risks. The old adage *everything in moderation* is especially relevant when it comes to artificial sweeteners. So enjoy them, but don't overdo it!

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Anxiety, Depression, and Diabetes Burnout

Introduction

Diabetes, as you are well aware, is a very complex illness with many potential complications. But the psychological complications of diabetes tend to be much more subtle and, as a consequence, more difficult to detect than the physical complications. Nonetheless, it is possible, using research-based psychiatric critera, to diagnose and treat these psychological conditions.

Anxiety, depression, and diabetes burnout are some of the more common psychogical disorders faced by diabetics. Indeed, there is a higher prevalence of anxiety and depression among diabetics than among the general public (1-3). We will delve into these conditions one by one, starting below with anxiety.

Anxiety

Characterized by a state of inner dread and turmoil, anxiety is similar to fear, which is a response to a specific threat. However, anxiety is rooted in a pervasive feeling of "impending doom," and, unlike fear, isn't necessarily triggered by one particular stimulus. Some fear is actually a good thing, as it helps you to remain vigilant against a perceived danger. However, when the perceived sense of dread becomes chronic, and occurs even in the absence of real danger, it can lead to anxiety disorders.

Diabetes increases the likelihood of being diagnosed with anxiety disorders and anxiety symptoms, and can leave patients feeling that they have lost control of their lives.[5-7] Factors that may heighten anxiety in diabetics include:

The routine. Diabetics have to constantly monitor their sugar levels throughout the day, every day, keeping them in a state of continual alertness.

The fear: Diabetics often have ongoing apprehension about blood sugar issues and hypoglycemic events.

The futility: Diabetics have to inject insulin for the rest of their lives. This can be disconcerting to some patients.

The complications: Peripheral neuropathy, vision problems, and swelling are some of the complications that may eventually arise in a long-term diabetic; this may cause patients to perseverate excessively on the future.

How does anxiety manifest?

Now that we have some idea of the reasons a diabetic might experience anxiety, it is important to understand how anxiety manifests itself. Anxiety symptoms include restlessness, diarrhea, irritability, concentration problems, shortness of breath, sweating, and 'feeling on edge'.[8] If you are experiencing any of these symptoms you should report them to your physician immediately.

Anxiety over finger prick sugar test and insulin injections

Insulin injections are an unavoidable part of life if you are a type 1 diabetic. Insulin is also required for type 2 diabetics when other treatments are no longer effective. Although insulin injections provide essential control of blood sugar, the idea of injecting yourself with a needle for the rest of your life isn't especially inspiring. Combine that with the ceaseless pricking of one's fingers to measure blood sugar levels and you can see how a patient might become distressed.

Research reports consistently on the general fear and aversion experienced by diabetics towards insulin injections and blood sugar monitoring.[9,10] This discomfort is a pervasive problem, as attested by a 2009 patient survey, which found that many diabetics would prefer to have fewer injections per day.[11] And because these injections and finger pricks are sources of anxiety, in extreme circumstances they may lead to an avoidance of treatment.[12] Worse still, this anxiety may prevent newly diagnosed diabetics from beginning insulin therapy in the first place.[13] More information on the phenomenon of treatment avoidance (known as 'diabetes burnout') will be presented later in this chapter.

Addressing anxiety

If left untreated, daily anxiety can develop into a disorder and/or lead to depression. This means that the sooner your anxiety is diagnosed and addressed, the more likely you are to avoid a serious negative outcome.

Once symptoms of anxiety have been observed, the first person to consult is your physician. Having been informed of the symptoms, he or she can initiate the

appropriate treatment measures, including therapy and medication. Other activities you can engage in if you are anxiety-prone include breathing exercises, yoga, meditation, and physical exercise.[14-16]

Many diabetics experience symptoms of depression, and a significant number suffer from a serious, chronic form of this disorder, possibly triggered by the heightened sense of anxiety diabetes inspires.[4]

Depression

Did you know that symptoms of depression affect more than 30 percent of diagnosed diabetics and that 10 percent of these individuals will slide into a serious, major depression?[4] Feelings of depression or sadness are experienced by everyone at least once during their lifetime, as the odd bad day or experience of feeling down on your luck is normal; however, when these feelings persist over long periods of time, they can develop into serious psychological problems. Depression, observed in many diabetics, needs to be diagnosed, addressed and treated appropriately.[17-20]

Not only do patients with diabetes-related depression tend to require healthcare services more than individuals with diabetes alone, but they also experience increased mortality rates.[21,22] Furthermore, diabetics dealing with depression experience a pronounced increase in adverse medical symptoms, compared with their non-depressed diabetic counterparts. Consequently, it is important to be vigilant about depression and to address it at its earliest stages.[23,24]

Which comes first? Depression or diabetes?

The question is a lot like that of the chicken and the egg. Although research has demonstrated that there is a strong correlation between diabetes and depression, it is difficult to work out, in general, which of the two comes first. Research indicates that individuals dealing with serious depression are at a higher risk of developing diabetes.[25-27] However, individuals with type 1 or type 2 diabetes are also more prone to developing serious depression.[28]

One of the common denominators connecting diabetes with depression is *emotional stress*, which is linked to the development of diabetes but is also a contributing factor in the onset of depression.[29] It is important to address this viscous circle, in order to limit the back-and-forth damage between the two illnesses.

How does depression feel?

Depression isn't just a low-energy condition associated with moodiness. Other symptoms include excessive fatigue, overeating or loss of appetite, loss of interest in hobbies, an inability to concentrate, difficulty making decisions, feelings of guilt and/or helplessness, and thoughts of suicide.[30] If these symptoms persist, a health care provider must be notified. The opinion of your doctor or psychologist is key to proper assessment of your condition and the commencement of appropriate treatment.

Depression as a risk for poor diet and self-care, and for non-compliance with medical treatment.

Because suicide and depression are intimately linked, it is important to address depression early on. But there other factors that need to be considered: a poor diet, diminished self-care and non-compliance with medical treatment are all connected to the issue.[31-33]

When patients suffering from a chronic illness become depressed, it can be hard for them to manage their illness. Suddenly, instead of dealing with one health concern, they find themselves having to manage two conditions. Moreover, depression makes it difficult to function at your optimum, as symptoms of the illness usually include low energy levels and diminished concentration. These circumstances may make it difficult for a diabetic to keep track of their medication scheduling, prepare their meals, and inspect their feet for any abrasions, which can potentially become ulcers. In other words, comorbid depression and diabetes can send a patient on a steadily downward spiral.[34,35]

Dealing with depression

If both depression and diabetes are present in a patient, it is important to address the two issues immediately. Should you be experiencing symptoms of depression, arrange an appointment with your doctor to discuss them. Antidepressant medications and/or psychotherapy can lead to profound improvements in your situation.[36-38]

In addition to getting help from a mental health professional, there are simple, everyday lifestyle changes you can adopt to help improve your situation. Even though it may be difficult to initiate, exercise has been found to be beneficial in

treating depression.[39,40] Other treatments found to improve depression include yoga, and mindfulness meditation.[41-43]

Diabetes Burnout

The term burnout is often used when a person has exhausted her capacity to carry out the necessary responsibilities for work, school and/or relationships. It often occurs as a result of long, uninterrupted focus on a particular task or situation, which ultimately robs an individual of her physical, emotional and intellectual ability to pursue her objectives.

This phenomenon also occurs among diabetics. Diabetic burnout is a troubling situation stemming from the frustration and angst connected with a diabetes regime, often resulting in dangerous behavior whereby diabetics ignore their blood sugar levels and abandon their diabetes medicine.[44]

It's a question of freedom. Many long-term diabetics begin to feel they are being controlled by the disease and stripped of their liberty.[45] Diabetes burnout is a reactionary impulse leading not only to a rejection of diabetes medications and insulin, but also to a refusal to continue with a healthy diabetic diet and exercise. Even worse, many diabetics, in the throes of burnout, spurn help and stop visiting their doctor. Feeling defeated by the disease, they lose their motivation to continue fighting against the disease.[44] Unfortunately, ignoring your diabetes for an extended period of time can have grave consequences, including poor glycemic control and worsening complications, such as the possibility of falling into a diabetic coma.

Since diabetes burnout is potentially life-threatening, it is of crucial importance to prevent this condition from taking hold. Mindfulness-based cognitive behavior has been recognized as an important means of helping diabetics take back control of their lives.[46,47] Experts also recommend trying new diets and exercises.

Conclusion

Depression, anxiety, and burnout are common comorbidities associated with diabetes, and need to be addressed as early as possible. Otherwise, these conditions can lead to severe exacerbations and/or complications of diabetes. Therefore, if you are experiencing any of the symptoms mentioned above, contact your doctor immediately.

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Sleep and Diabetes

Introduction

In today's rapid-paced world, a good night's sleep can feel more like a luxury and less like the priority that it is intended to be. Surrendering to Hypnos, the god of sleep, and sliding into his realm of dreams is a restorative process designed to balance your moods, recharge your batteries, and allow you to perform at your optimum level the next day. Of even greater importance is the role sleep plays in maintaining your long-term health and well being; evidence suggests that poor sleep quality or sleep deficit can increase the risk for developing certain medical conditions.

Perhaps you enjoy burning the candle at both ends, and because of your fast-paced lifestyle, you seldom get the eight of hours of shut-eye you need. Well, did you know that sleep deficiency can develop into sleep disorders that are associated with heart disease, stroke, high blood pressure, depression, attention deficit hyperactivity disorder (ADHD), obesity, and type 2 diabetes?[1]

Sleep deprivation is a growing public health epidemic, which is increasingly prevalent in children.[2,3] Recognized as contributing to obesity and as a risk factor for type 2 diabetes, lack of sleep and disruption of your circadian rhythms (the 24 hour biological clock that determines our state of sleepiness) are associated with metabolic disturbances that affect energy balance, food intake, inflammation, and insulin sensitivity.[4]

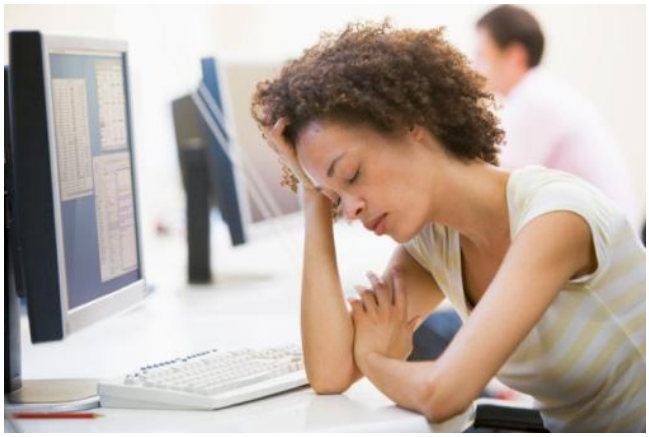
Poor sleep quality stems from insufficient sleep, fragmented sleep, obstructive sleep apnea (OSA), and circadian disruptions.[5] These sleep deficiencies can adversely affect glucose metabolism, leading to pre-diabetes. Pre-diabetes and diabetes can then exacerbate sleep disorders.[6]. Therefore, it's a bit of a "chicken and egg" scenario.

This chapter aims to understand how sleep deficiencies can alter your metabolism and elevate your risk for type 2 diabetes. The emphasis is on sleep disorders among individuals who already have diabetes, and how poor sleep can exacerbate their conditions.

Types of Sleep Deficiencies

Sleep Deprivation and Fragmentation

In today's fast-paced, technology-saturated world, getting less than the recommended night's sleep has become the norm for many people. For some, it has even become a kind of status symbol, reflecting a full and busy life. Although sleep is often the first thing to go when we make sacrifices for our hectic lifestyles, the consequences of sleep deprivation are beginning to manifest themselves in the growing obesity epidemic and the increasing incidence of type 2 diabetes.[3,7]



Diminished sleep and poor sleep quality affect several hormones that affect blood glucose levels and metabolic pathways.[7] Sleep/wake cycles are interconnected with the concentration of leptin and ghrelin hormones that regulate hunger and appetite. Leptin is the appetite-regulating hormone that inhibits hunger, and that peaks during the evening when you are sleeping.[7] The interconnection between sleep/wake cycles and leptin and ghrelin can affect regions in the brain that control your cravings for high-calorie foods, which lead to obesity (see more in *Disruption of Circadian Rhythms).*[2]

Leptin has been shown to decrease in healthy young men after having only 4 hours instead of 10 hours in bed.[5,8] In contrast, levels of ghrelin (a hormone that increases appetite)are increased after sleep restrictions, and are associated with increased

hunger as well as greater consumption of unhealthy snacks and junk food.[5] Eating behavior is reportedly affected by sleep loss, with a greater tendency for night-time eating or consuming more calories after dinner, resulting in weight gain.7 Furthermore, genes that promote obesity appear to be activated under sleep deprivation.[2]

Heightened diabetes risk resulting from sleep loss is related to abnormal glucose metabolism. Several studies have demonstrated that lack of sleep leads to reduced insulin sensitivity, along with increased levels of the "stress" hormone cortisol.[3] Experiments with healthy subjects showed that an accumulation of sleep debt could decrease insulin sensitivity by up to 24%, reducing glucose tolerance and increasing the risk for diabetes.[5] Further proof has been accumulated by epidemiological studies with follow-up analyses of 5 to 17 years, associating an increased incidence of diabetes with short sleep duration.[5] It has also been shown that poor sleep quality can even include too much sleep, which can increase the risk of diabetes as well.[9]

Sleep fragmentation is the true mark of poor sleep quality. It is characterized by a difficulty in maintaining sleep throughout the night- sleep is easily interrupted and/or total sleep time is less than normal. Insomnia, depression, fatigue, living in a noisy area, and having symptoms of anxiety can all readily cause sleep disturbance, which has been implicated as a predictor of type 2 diabetes.[5,10] A few studies have also associated poor sleep quality with poor glycemic control.[5]

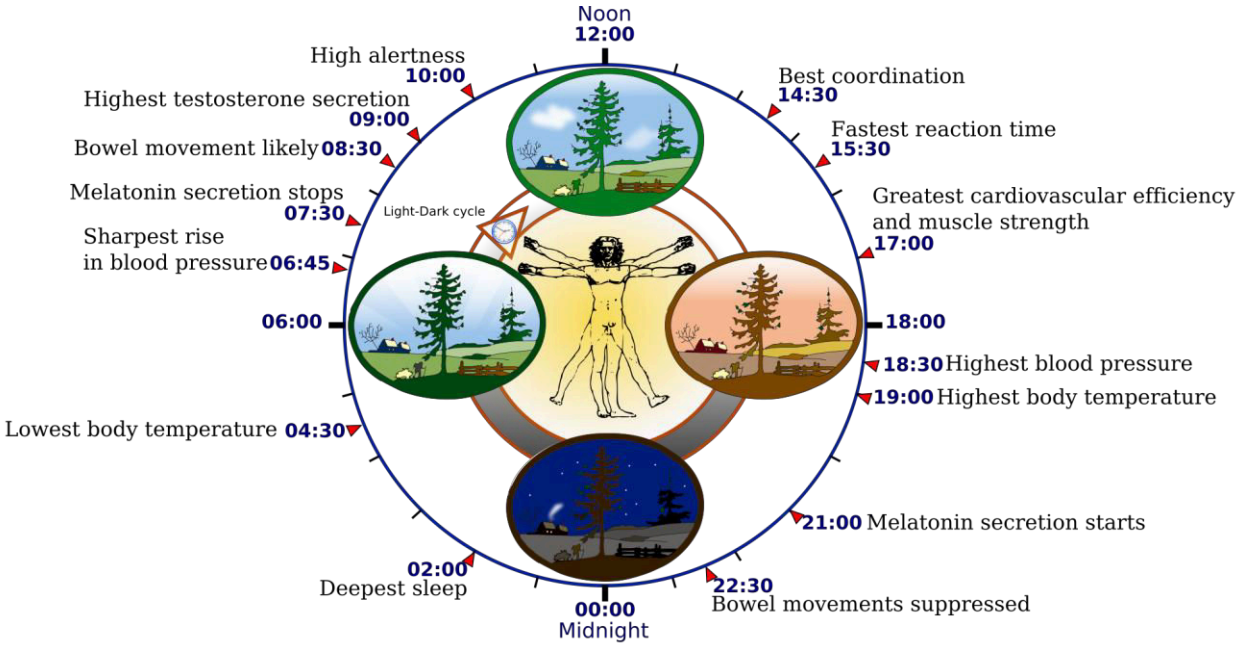
In a more recent study, poor sleep quality increased the levels of circulating free fatty acids. Changes in free fatty acid levels in the blood contributed to decreased insulin resistance, which led to increased diabetes risk and metabolic disorders.

When healthy young men were subjected to restricted sleep, their levels of free fatty acids were elevated and their insulin sensitivity was reduced.[11]

Sleep loss appears to affect the lipolytic hormones responsible for fat breakdown, leading to increased circulating levels of free fatty acids, which can result in insulin resistance.[11] These findings demonstrate the need for interventions in sleep behavior, in order to lower the risk of weight gain and of type 2 diabetes.[3] The good news is that even long-term sleep debt can be repaid, although it will take more than a couple of weekends to catch up.[12]

Disruption of Circadian Rhythms

Commonly referred to as our "biological clock," circadian rhythms are the physiological and behavioral changes that occur over the course of each 24-hour day in response to light patterns. Circadian rhythms affect sleep/wake cycles, fasting/feeding cycles, hormone release, body temperature, and metabolism.[5,13] Disruption of these rhythms, caused by nightshift work or other activities mismatched to the time of day, can lead to metabolic dysregulation.[5] Circadian misalignment is best exemplified in people performing shift work, who sometimes eat meals during times that are scheduled for sleep by natural circadian schedules. Not only does shift work invert the activity-rest cycle, but it can also lead to sedentary behavior accompanied by stress and an increased intake of unhealthy foods.[14]



Feature of the circadian rhythm

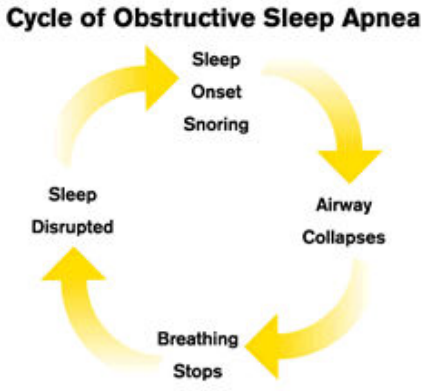
The levels of hormones involved in metabolism, such as leptin, are also affected by circadian rhythms. Melatonin, another hormone, regulates sleep/wake cycles and has been connected with glucose metabolism. Melatonin production is at its peak during sleep, but it is suppressed during daytime.[15] A research study showed that women with low nighttime levels of melatonin had twice the risk of developing type 2 diabetes. In addition, genetic mutations leading to low melatonin signaling can result in impaired insulin sensitivity and type 2 diabetes.[15]

Animal studies have highlighted melatonin supplementation as a potential therapy. Rats that ingested melatonin were protected from diabetes, and had improved cholesterol levels.[15] Melatonin supplementation was also extended to human subjects, in a small study that treated middle-aged individuals with insomnia and type 2 diabetes. Melatonin was taken nightly over 3 weeks, improving their ability to sleep, though without causing significant changes in glucose metabolism.

Further studies are required to see if melatonin treatment can reduce the risk of type 2 diabetes, and if it is able to safely improve glycemic control.[16]

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is a common disorder wherein breathing is paused for a few seconds or minutes several times during the night.[17] In patients with OSA, the airways are blocked or collapse, leading to intermittent hypoxia, where the lungs do not receive sufficient oxygen. Normal breathing resumes after these intermittent pauses, producing a loud snort or choking sound.[17] In patients with OSA, the quality of sleep is disrupted and shallow, and generally ends in a reduced amount of total sleep.



There is evidence that hypoxic stress (deficiency in oxygen) related to OSA may have adverse effects on glucose metabolism and diabetes risk.[5] OSA is also associated with obesity, which can predispose individuals to insulin resistance. Strong connections between OSA and insulin resistance were found in large population-based studies, which showed that OSA increases the risk for abnormal glycemic control and diabetes. Furthermore, a pivotal study demonstrated that the degree of insulin resistance relates to the severity of OSA; mild OSA corresponded with a low degree of insulin resistance, whereas severe OSA correlated with higher insulin resistance.[18]

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Gestational Diabetes and Sleep Disturbances

Sleep patterns during pregnancy alter as a result of hormonal and physical changes. Women in their first trimester usually experience excessive sleepiness. By their third trimester, they experience an increase in sleep disturbances, sometimes with snoring indicative of OSA, particularly among women with a BMI above 25kg/m^2. Multiple studies have linked OSA symptoms with gestational diabetes, which can result in negative outcomes for both the mother and baby, such as preeclampsia, hypertension, and premature births.[5]

People with Diabetes and Sleep Disorders

For people who already have diabetes, sleep disturbances are a common complaint. Poor sleep can exacerbate diabetes and affect mental wellbeing. However, sleep management techniques may help to improve the quality of life for these individuals. Rapid changes in blood glucose levels can provoke more awakenings during sleep among those with type 1 diabetes.[19] Meanwhile, drops in blood sugar levels may dampen the awakening response in people with type 1 diabetes and may lead to a hypoglycemic (low blood glucose) state that requires immediate attention.[20] If you are experiencing these symptoms, you may require monitoring of glucose levels throughout the night, and your doctor may need to adjust your blood glucose targets to avoid such episodes.[20] Individuals with diabetes may also have a frequent need to urinate throughout the night, and/or they may experience neuropathic pain, which can disrupt sleep and exacerbate sleep deprivation.[6]

Poor sleep can also have a negative impact on glycemic control in people with type 2 diabetes, in whom the effects of interrupted sleep and insomnia can result in

higher fasting glucose levels and insulin resistance.[5] This poor sleep may be attributed to obesity or obesity-related conditions, such as OSA. There are several studies showing that OSA affects 58% to 86% of obese individuals with type 2 diabetes. Despite this frequency of occurrence, OSA is often unrecognized, leaving many people untreated for it.[21] Because OSA is also associated with inflammation and oxidative stress, individuals with OSA on top of their diabetes may experience further complications, such as peripheral neuropathy, retinopathy and nephropathy.[5,22,23] Research is currently underway to assess whether treatment of OSA improves glycemic control and impedes the onset of microvascular complications.[5]

Type 2 diabetes individuals may suffer from sleep problems due to restless legs syndrome (RLS). Pain associated with polyneuropathy can also develop into RLS (24). Restless legs syndrome (RLS) is when you get an uncomfortable urge to move your legs, and is often partnered with other sensations of tingling or pain that can make it difficult to maintain sleep.

Treatment Options

Sleep disorders, such as insomnia, require appropriate therapy from health professionals or specialists at a sleep clinic. Good sleep hygiene, behavioral management, and medications may help to treat these sleep disorders.[25] Interventions to prevent the development of type 2 diabetes may involve adding

back hours of sleep throughout the week and/or the weekend to make up sleep debt, along with the establishment of a regular sleep schedule.[26]

Current treatment options have largely focused on correcting OSA to prevent diabetes risk or alleviate existing conditions. Treatment of OSA involves keeping the airways open by continuous positive airway pressure (CPAP). This mandates the use of a CPAP machine, which blows air into a tube connected to a mask covering your nose and/or mouth.

The efficacy of diabetes management by CPAP remains inconclusive due to inconsistencies between study designs and criteria.[5] However, CPAP treatment may have potential benefits for glucose metabolism among individuals with prediabetes.[27] Further treatment of OSA may involve weight loss interventions to alleviate symptoms in obese individuals.[28]

Conclusion

Sleep has steadily been ignored as a priority in our busy lives. However, if it is neglected for too long, sleep might have serious and adverse consequences for your health. Several studies have demonstrated that disturbed sleep is associated with abnormal glucose metabolism, obesity and type 2 diabetes. Therefore, diabetes

treatments and preventative techniques are beginning to take into account the importance of sleep quality, by incorporating interventions to correct sleep debt and OSA.

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Diabetes Medications

Introduction

Making sure your blood sugar levels remain within the range recommended by your doctor can be challenging. It depends very much on vigilance, since your blood sugar levels can change for many different reasons, sometimes unexpectedly.

Where diet and exercise aren't enough to help you manage your diabetes, insulin and other diabetes medications can assist you, by helping to lower blood sugar levels. But keep in mind that the effectiveness of these treatments is highly dependent on the timing and size of the dose. And don't forget that any medications being taken for other health-related conditions may adversely affect your blood sugar levels. Therefore, always verify the potential side effects of your meds with your doctor.

There is a wide array of medications used for the treatment of diabetes; however, treatment varies according to the type of diabetes you are diagnosed with. In type 1 diabetes, the pancreas is no longer able to make insulin, and the only way to treat this condition is to inject insulin or to use an insulin pump. In type 2 diabetics, insulin may still be produced by the pancreas in the early stages; therefore, these patients are instructed to modify their lifestyle by changing their diet and engaging

in exercise. Later on, patients with type 2 diabetes may be given oral diabetes medications, which potentiate the effects of insulin.

Lifestyle changes have been found to be more effective than medication.[1] However, individuals with type 2 diabetes may have to resort to using insulin injections if their sugar levels are not kept under control. In type 2 diabetics, insulin can be added to pre-existing oral medications. It is important not to take greater amounts of insulin than the dosage prescribed. This can cause severe hypoglycaemia, which may also occur if insulin is not taken at the recommended times, and if meals are skipped. Taking the physician-prescribed dosage of insulin enables the right amount of glucose to be taken up by cells.

The brain uses a large amount of glucose, and when no glucose is available in the bloodstream, the brain has no energy source. This can lead to fainting spells and even coma. Therefore, administration of insulin must be done with caution, and insulin must be taken at the dosages and times prescribed by the physician. The physician must always be consulted prior to making any changes in medications.

Insulin

There are many types of insulin, and they differ in terms of their onset (the time it takes for the insulin to reach the bloodstream), duration (how long the medications work for), and peak (when the insulin reaches its maximum potential/strength). There are ultra-rapid-acting, rapid-acting, short-acting, intermediate-acting, long-acting, ultra-long acting, and pre-mixed insulins. Insulin cannot be taken in pill

form, as it would be metabolized; therefore it must be injected into the fat underneath the skin.

The insulin pump is a small device connected to a catheter, which is put under the skin. The pump dispenses insulin as programmed, and a constant dose of insulin is pumped throughout the day; more insulin is programmed to be dispensed during meal times.[2] Insulin is also available in an inhaled form.[3] If insulin is started on type 2 diabetics when plasma glucose concentrations are still at lower levels, improved goal attainment is observed.[4]

The above is just a brief overview of the different modes of insulin administration. The following section will give you more detailed information on what's available when it comes to insulin therapy.

Rapid-Acting Insulin

This type of insulin will start to work 15 minutes after being injected, and it will continue to work for 3-5 hours. Rapid-acting insulins are great to take 15 minutes prior to a meal, or even after a meal. Some examples of rapid-acting insulin are: insulin aspart, insulin glulisine, and insulin lispro.

Studies have found rapid-acting insulin use to be beneficial.[5] The addition of insulin aspart can help potentiate existing therapies for glycemic management. It

was observed that when individuals were unable to attain good glycemic control with oral antidiabetic medications and long-acting insulin, the addition of insulin aspart to their treatment at one or more meals intensified the therapy.[6] Also, in older individuals with diabetes, treatment with insulin aspart seemed to improve post-meal glucose levels, confer long-term metabolic control, reduce the risk of becoming hypoglycemic overnight, and increase patient satisfaction.[7]

Short-Acting Insulin

The short-acting insulins start working around 30-60 minutes after entering the bloodstream, and continue to work for around 5-8 hours. They are injected approximately 30-45 minutes *before* having a meal. This type of insulin is called regular insulin. In type 2 diabetics with insulin resistance, treatment with regular insulin was associated with patient satisfaction and adherence.[8] In addition, it was seen to improve plasma glucose levels; however, it also causes weight gain.[9] If you are taking this medication and notice weight gain, you should report it to your physician on your next visit. He/she will then be able to adjust your medications if need be.

Intermediate-Acting Insulin

This class of insulin starts to work in around 1-3 hours, and works for 12-16 hours. Intermediate-acting insulin is called NPH insulin, which stands for Neutral Protamine Hagedorn. In general, NPH is not as cost-effective as other types of insulins, and is associated with a greater incidence of hypoglycemia.[10,11] Compared

to long-acting insulin glargine, NPH insulin posed a higher risk of hypoglycemia during sleep, and was not as beneficial in those with long-lasting type 2 diabetes.[12]

Long-Acting Insulin

Long-acting insulin begins to work an hour after injection, and works for 20-26 hours. Two insulins in this category are: insulin glargine and insulin detemir. Insulin glargine has been shown to be better than NPH insulin, as it is associated with a lower incidence of hypoglycemia during sleep, less weight gain, and greater benefit for patients who had a longer duration of type 2 diabetes.[12-14] Additionally, in type 1 diabetics, taking insulin glargine was associated with lower levels of fasting plasma glucose, as well as fewer hypoglycemic episodes when compared to treatment with NPH.[15] Compared to insulin glargine, insulin detemir lowered blood sugar more consistently, while glargine was more variable according to those with type 1 diabetes.[16] This means that the effects of insulin detemir will not vary as much from person to person for a given dose. Insulin detemir has also been shown to produce lower weight gain than insulin glargine; however, they both had similar effects on glycemic control.[17]

Pre-Mixed Insulins

Pre-mixed insulins are solutions containing a mixture of rapid- or short- acting insulin and intermediate-acting insulin. It consists of insulins with different onsets and durations, and will function according to the attributes of the insulins it contains. There are different varieties of pre-mixed insulin, distinguished by the types of insulin they contain, and the percentage of each type. The name of the

solution reflects these percentages. For example, a half-and-half mixture of NPH insulin with regular insulin will be labeled with the name of the medication, followed by 50/50. If there was a combination of 70% NPH with 30% regular, you would have 70/30. The 70/30 combination of NPH and regular insulin starts to work approximately 30 min to an hour after injection, lasting for about 10-18 hours. Other combinations are NPH insulin with rapid-acting insulins such as insulin aspart or insulin lispro. When the rapid-acting insulins are combined with the NPH, the onset is quicker (around 15 minutes) and it lasts for 10-18 hours. The 70/30 mixture of NPH insulin and insulin aspart was seen to be more effective at decreasing the sugar rise after a meal than the mixture of NPH insulin with regular insulin.[18]

Hypoglycemic events were reported to be lower in type 2 diabetics after starting on pre-mixed solutions.[19] When pre-mixed insulin did not lead to better diabetes control, then glycemic control and low hypoglycemic events could be achieved with insulin glargine and oral anti-diabetic medications.[20,21] Therefore pre-mixed solutions may be beneficial in some patient populations, but not in others.

Advances in Insulin

Since insulin is very important in the treatment of diabetes, new types of insulin are continually being formulated and studied. Although insulin allows diabetics to function effectively, it has its limitations. One of the most common adverse effects of insulin is hypoglycemia, either during the day or during sleep. This usually happens when a meal is skipped or when a larger-than-recommended dose is taken by the patient. Another limitation of insulin is that it needs to be taken at a fixed time every day. This can pose a problem for many people as they may be busy at

scheduled times, or might occasionally forget. A third limitation is the fact that insulin must be injected. For some people, it is bad enough to go to the doctor for vaccinations or to receive a shot of medication once in a while – but imagine having to give yourself an injection on a regular basis. Many individuals do not particularly like these features of insulin. Therefore, research is being conducted to address these limitations.

The pill form of insulin will be groundbreaking, as it will eliminate the need for needles. This development remains a challenge, however, as the pill needs to be made in such a way that it won't be metabolized by the body. Clinical trials are currently being carried out on insulin pills.

Anti-Diabetic Oral Medications

Oral medications are mostly used to treat type 2 diabetes; however, some of these drugs can be used with type 1 as well. The medications usually function by making cells increasingly sensitive to the insulin produced by the body, or else they enable the body to make more insulin. Some oral medications slow down the digestion of food, so that sugar from the food is introduced into the bloodstream at a slower rate.

Ultra-Rapid-Acting Insulin

One of fastest insulins available now is the ultra-rapid-acting insulin. This type of insulin will start to work very fast (in less than 15 minutes). Studies have observed that ultra-rapid insulin was more effective than other types of insulin at reducing the increased glucose levels seen in type 1 diabetics after meals.[22] With Type 2 diabetics, it was revealed that an inhaled form of this ultra-rapid acting insulin could effectively decrease the post-meal rise in glucose.[23] Since it is absorbed quickly by the lungs in 14 minutes, the inhaled form can have an effect on the elevated glucose in the blood after a meal.[23] This form of insulin is great for those who do not wish to poke themselves with a needle; however, patients need to be screened for lung problems to confirm whether it can be safely used.

Ultra-Long-Acting Insulin

Among the newer insulins are ultra-long-acting insulins, including insulin degludec. This type of insulin diffuses into the blood stream at a slower rate than others, and has a longer half-life (the time it takes for half of it to degrade) resulting in a stable glucose- lowering effect.[24] Insulin degludec is observed to reduce the number of episodes of hypoglycemia during sleep, tighten glycemic control, and offer greater flexibility in the administration time.[25] Since it is released slowly, insulin degludec can be administered anytime during the day, provided it is taken once daily. This is because even when insulin degludec is taken at a varied schedule, glycemic control remains intact.[26]. Furthermore, insulin degludec has been shown to be more consistent in lowering glucose levels than insulin glargine in individuals with type 1 diabetes.[27]

In general, insulin degludec is well tolerated, yields a low rate of hypoglycemic events, is safe, and is also great for those who aren't able to take insulin at the same time every day.

Sulfonylureas

The sulfonylureas are medications that work on the beta cells of the pancreas, and stimulate those cells to release insulin. However, when the beta cells stop functioning, sulfonylureas are no longer effective. Therefore, they are used in the earlier stages of type 2 diabetes. Some of the older first-generation sulfonylureas are: chlorpropamide, tolbutamide, tolazamide, and acetohexamide. Second-generation drugs include glipizide and glyburide (also known as glibenclamide). These are more potent than the first generation drugs.[28] An example of a third-generation drug is glimepiride.

Since sulfonylureas stimulate the release of insulin, one of their potential side effects is hypoglycemia - especially with chlorpropamide and glyburide, as these bind to plasma proteins and stay in the body for longer.[29,30] Hypoglycemia usually comes about if a higher-than-recommended dose is taken, or if the patient abstains from eating. First-generation sulfonylureas are known to cause more severe hypoglycemia than other generations. For instance, patients who were given glimepiride had fewer hypoglycemia events when compared to those of glyburide.[31] A fourth-generation sulfonylurea has emerged in recent years to help avoid hypoglycemic events. This is known as JB253, a prototype drug that is activated when exposed to blue light. This drug design allows JB253 to be turned "on" or "off" by a light switch and has shown promising results on pancreatic cells in a laboratory setting.[32] Future therapy with JB253 may prevent unfavorable

hypoglycemia events that are associated with sulfonylurea use, since it grants the patient control over when insulin will be released.

It has been proposed that sulfonylureas, particularly tolbutamide, may cause destruction of the beta cells of the pancreas by causing the cells to self-destruct.[33] However, more research needs to be done to further investigate this possibility.

Meglitinides

Meglitinides work by stimulating the release of insulin from the pancreas.[34] These drugs were seen to induce a faster and greater rise in insulin than some sulfonylureas.[35] While they start to work faster than sulfonylureas, they only work for a short time; therefore, they are primarily used to lower glucose levels after a meal.[34] Some examples of these drugs are repaglinide, mitiglanide and nateglinide.[35] These medications confer a lower risk of hypoglycaemia than sulfonylureas, since they have a shorter duration of action.[34]

Biguanides

Metformin comes under the class of biguanides, and is the only drug in this category at the present. Decades ago, the biguanides phenformin and buformin were used in the treatment of diabetes; however, they caused lactic acidosis and were subsequently withdrawn from circulation.[36,37] However, metformin has been shown to have similar efficacy to phenformin, only without the severe lactic acidosis. Overweight diabetics using metformin also had less weight gain and less hypoglycemic episodes.[38]

Metformin works by making cells more sensitive to insulin, so that glucose in the blood can be taken up by cells.[39] Another function of the drug is to stop the production of new sugar by the liver.[40] Since it doesn't achieve its effects by increasing the release of insulin, metformin has also been used in type 1 diabetes treatment. Overweight type 1 diabetes patients taking metformin, in addition to their daily insulin, needed a smaller daily dosage of insulin, and showed evidence of weight loss.[41] Despite the association of metformin with lactic acidosis under certain conditions, the drug has regardless been shown to lower mortality.[42]

Thiazolidinedione

Thiazolidinediones work by increasing the action of insulin, decreasing insulin resistance, and reducing the elevated fatty acid levels seen in insulin-resistant patients.[43,44] Some examples of thiazolidinediones are: Rosiglitazone, Pioglitazone, Lobeglitazone, and Troglitazone. Among the less favourable effects of these drugs is potential weight gain.[45-47] Another adverse effect is liver injury, and an increase in liver enzymes has been associated with some thiazolidinediones. Therefore, the liver enzymes of patients taking these medications are often checked regularly.[48-50]

Bone loss is another associated risk of thiazolidinedione use, and this increases the risk of fracture, seen predominantly in postmenopausal women.[51-54] Rosiglitazone has also been associated with an increased risk of heart attack.[55,56] Recently a new thiazolidinedione called rivoglitazone has been developed; however more studies need to be done in order to fully assess its risks.[57,58]

Alpha-Glucosidase inhibitor

This group of drugs inhibits the enzyme alpha-glucoside. This enzyme is responsible for breaking down sugars into smaller molecules so that they can be metabolized. When this enzyme is blocked, the breakdown of sugar in the intestine is slowed, leading to a delayed absorption of sugar.[59] Studies in animals showed that treatment with alpha-glucosidase inhibitors can also delay diabetes complications such as kidney disease and neuropathy.[59] Some examples of drugs in this category are: Acarbose, Miglitol, and Voglibose. Some of their most pronounced side effects are abdominal pain, diarrhea, and flatulence, although these improve with regular use.[60] Gradual initiation into treatment using low doses should help to minimize these side effects.[61]

Amylin Analogs

Amylin is a hormone secreted alongside insulin by the beta cells of the pancreas.[62] Therefore, when the beta cells stop working, both insulin and amylin fail to be secreted. Amylin functions to delay the processing of food in the intestine, thereby decreasing the amount of sugar in the blood stream following food intake.[63] This hormone also inhibits glucagon, a hormone that raises the amount of glucose in the bloodstream.[62]

Pramlintide is an amylin analog used in the treatment of diabetes. People with type 1 and type 2 diabetes, who used pramlintide in addition to insulin, experienced weight loss and decreased plasma glucose levels.[64-66]

Dipeptidyl Peptidase-4 Inhibitors

The enzyme dipeptidyl peptidase 4 (DPP-4) deactivates two hormones involved in potentiating insulin functions. These hormones are glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotrophic polypeptide (GIP).[67] GLP-1 stimulates insulin secretion, suppresses glucagon secretion, delays gastric emptying, and reduces appetite.[68] Therefore DPP-4 inhibitors reduce the function of DPP-4 and thereby allow the functions of GIP and GLP-1 to continue. Some examples of DPP-4 inhibitors are: sitagliptin, vildagliptin, linagliptin, and saxagiptin. The addition of DPP-4 inhibitors to metformin therapy seems to improve plasma glucose levels in people who weren't able to achieve glycemic control with metformin alone.[69] These DPP-4 inhibitors were found to be cardioprotective, as heart attack frequency was reduced in patients taking these drugs.[70,71] On the other hand, some studies have shown that taking DPP-4 may increase the incidence of pancreatitis; however, more research is needed to verify this claim.[72,73]

Glucagon-Like Peptide-1 Receptor Analogues or Incretin Mimetics

A newer class of drugs are the incretin mimetics, or GLP-1 receptor agonists, that are used to treat Type 2 diabetes. The hormone GLP-1 stimulates insulin secretion, suppresses glucagon secretion, delays gastric emptying, reduces appetite, and improves plasma glucose levels.[68] GLP-1 receptor agonists are designed to replicate these effects, by 'mimicking' GLP-1. In fact, GLP-1 receptor agonists may function better than GLP-1; GLP-1 has a short duration of action, but its analogues work for longer periods of time.[68] These affect the same biochemical pathway as the DPP-4 inhibitors; they function by increasing the secretion of insulin, but without hypoglycemic side effects.[74] Combined with metformin, GLP-

1 receptor agonists are shown to be more effective at lowering plasma glucose levels compared to the combination of DPP-4 inhibitors and metformin.[74] Some examples of incretin mimetics are: exenatide, lixisenatide, taspoglutiee, albiglutide, and liraglutide.[75] Since incretin mimetics are rendered inactive by DPP-4, they are sometimes used in combination with DPP-4 inhibitors.[68]

However, it has been observed that insulin mimetics may cause damage to the pancreas.[76] Indeed, the use of incretin mimetics is associated with an increased risk of pancreatic cancer.[77] Despite this early evidence, further monitoring of patients taking these drugs is necessary before we can arrive at any definitive conclusion.[78,79]

New Developments: Beta Cell Regeneration

As mentioned earlier, insulin is secreted by the beta cells of the pancreas. When the beta cells' function is compromised, they cannot secrete sufficient amounts of insulin, and oral medications may need to be taken to boost insulin production. When the beta cells do not produce insulin at all, insulin injections must be taken.

Beta cell regeneration is a promising new therapy that can be beneficial in individuals without functioning beta cells. It would involve restoring the function of beta cells, and eliminate the need for some of the oral diabetes medications. Studies regarding this therapy are being conducted to examine the mechanisms by which beta cells might be regenerated.[88,81] At present, this therapy remains somewhat hypothetical; however, the future may bring with it some promising innovations.

Conclusion

Having discussed many currently prescribed diabetes medications, we can speak for the benefits that a number of mainstream drugs have had for patients. Many of these treatments are being modified in order to reduce their side effects and to make them more user friendly. Yet we also know that there is a big responsibility on the patients' part to take the medications as directed. For example, adhering to a diet low in sugar, low in saturated fats, low in sodium, and high in fiber, can greatly improve patient outcomes. Engaging in regular exercise will also help to lower sugar levels in the blood, as the muscles consume sugar in order to function. Finally, being overweight or obese can lead to insulin resistance; therefore, losing weight will also serve you well in your fight against diabetes.

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Advances in Diabetes Treatment

Introduction

Diabetes has been known about since ancient times. Throughout history, it has been the subject of intense study and the target of numerous treatment attempts. Modern treatments are often able to achieve effective and stable results; however, one of their greatest drawbacks is that they need to be taken for life. Therefore, methods that can prevent or even eradicate diabetes are currently under investigation.

Type 1 Diabetes Vaccine

Just as there are vaccines developed for viruses like polio, measles, and mumps, scientists are currently working on a vaccine to prevent type 1 diabetes.[1] Studies have shown that certain viruses are associated with type 1 diabetes, as individuals diagnosed with the disease were found to have viral genetic material in their system.[2-4]. It is thought that viral infection may alter the insulin-producing beta cells of the pancreas such that the immune cells of the body start to identify these pancreatic cells as foreign.[1,2] Once the beta cells of the pancreas are registered as foreign, they are attacked and destroyed by the immune cells, leading to diminished production of insulin.[2]

Evidence for the centrality of the immune system in protecting against diabetes comes from a variety of sources, including human medical history records. Type 1 diabetes diagnoses are more common today than in the past. One theory behind

this increased frequency is the "hygiene hypothesis". It proposes that poorer hygiene and sanitation practices in the past exposed us to a greater variety of germs and parasites, which would have stimulated the immune system and conferred protection against autoimmune diseases such as type 1 diabetes. [1, 5-7]

Gut bacteria may also play a role in protecting against diabetes, as these make up an important part of the immune system. It was observed that the composition of gut bacteria between diabetics and non-diabetics differed significantly.[6,8] Therefore, having the right exposure to certain microbes and parasites may contribute to the delay or prevention of autoimmune type 1 diabetes.

Protection against viruses and foreign agents is the ultimate goal of vaccines. Presently, vaccines that target the viruses associated with type 1 diabetes are being studied in animals; the results so far have been promising.[9]

Immunosuppressive Therapy

Another strategy for type 1 diabetes prevention may involve immunosuppressive drugs.[10] As a result of research showing that the immune cells of the body are responsible for attacking the insulin-producing beta cells of the pancreas, drugs that halt the action of fighter cells are thought to be helpful. Abatacept is one such drug. Studies have shown that abatacept delays the decline of beta cells and improves HbA1c levels, which reflect blood glucose levels.[10,11] However, further evaluation of abatacept is needed in order to fully validate the efficacy of this treatment.

Islet Cell Transplant

As discussed above, the beta cells of the pancreas produce insulin and are thought to be destroyed by immune cells in patients with type 1 diabetes. Therefore, one obvious way to fix this problem is to transplant new beta cells.

If you can get a kidney transplant when the kidney stops working, why not a beta cell transplant? In fact, this process has already been tried in humans. Following transplantation with donor beta cells, it was found that individuals started making their own insulin.[12,13] Patients were also seen to have decreased levels of HbA1c and did not report hypoglycemia which is caused by some medications.[12] However, most of the patients in these studies eventually needed to resume insulin injections several years after the transplant.[12] As with any transplant, the patients also needed to take immunosuppressive medications, which can cause side effects and complications such as infection, bone loss, and weight gain. More research is being conducted to see if we can modify the transplantation process so that individuals do not have to use insulin injections or immunosuppressive medications following transplantation.

A Bioengineered Pancreas

One of the newest outcomes in diabetes research is a bioengineered pancreas, which basically does the job of an ordinary biological pancreas.[14] This device does not suffer from many of the limitations of beta cells transplantation, which requires a donor and immunosuppressive drugs, and may only work for a limited amount of time.

One example of an artificial pancreas under development is the DRI BioHub.[14] This is an artificial pancreas bioengineered with real insulin-producing cells.[14] It is able to sense sugar levels in the blood stream, and then release insulin in the right proportions at the right time.[14] Current research aims to develop an artificial pancreas that can work for an extended period of time, without the need for immunosuppressive drugs.[14]

Conclusion

Diabetes is a complex disease, known to give rise to many debilitating complications. By now, science has developed a number of treatments that can help effectively control the condition. However, it may only be a matter of time before future developments are able to prevent, or even cure, diabetes.

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Conclusion

Medical experts all concur that the quicker you make the necessary lifestyle changes, the easier it is going to be to manage your blood sugar levels. It is an important fact for diabetics because the most challenging part of managing their disease is embracing a healthy lifestyle.

Although diabetes medications are an important component in controlling your diabetes symptoms, improved diet and exercise are keys to getting the upper hand on your condition.

The classic excuse that many diabetics use as a crutch for not committing to the necessary lifestyle changes they need to embrace is: *it's too late for me*. Often disappointment and frustration rest at the core of that resigned attitude. Maybe you've tried to lose weight in the past, or you were determined to exercise more consistently and more often. But for whatever reason, you were unable to stay disciplined, and you fell off the wagon. So you gave up, and you began to believe that there was nothing you could do to change your situation.

Well, the quicker you shake off the doubt, drop the negative attitude and quit being so hard on yourself, the better your odds of getting a handle on your diabetes. You can do it! Millions of others diagnosed with diabetes are successfully changing their lifestyles for the better. If they can do it, surely you are up to the challenge as well.

Making sound health choices is easier than you think. The road towards recovery is not long and arduous. The journey towards improved health begins with a single step in the right direction. And once you begin stringing a series of small steps together, you're going to be amazed by the distance that you've covered.

You are going to feel so much happier and fulfilled once you establish a committed attitude and buy into the improved lifestyle that your doctor recommends. Just imagine a life of increased energy and self-confidence. You can do it! Getting over that diabetes wall and beginning your new life where you are the master of your conditions instead of being enslaved by it, simply requires a change in attitude.

Rest assured the challenges that you are facing are not yours alone. Effectively dealing with your blood sugar issues is a whole lot easier once you establish an

effective support system that includes your physician and sympathetic family members and friends. When it comes to staying positive and fighting the good fight the more loved ones you have helping you with your battle, the better your odds of winning the war.

Let's face it; some days are going to be better than others. There are going to be moments when you slip up. It's only normal; you're human. Accidents happen, but that doesn't mean that you should beat yourself for making the occasional poor eating choice or missing a few trips to the gym. If you get too worked up and angry about what you haven't accomplished, you'll forget about all the good work you've already accomplished. And that kind of negativity can only spread, feeding your insecurities, and making it easier to neglect your long-term goals.

Believe it or not, the way you think, can have a huge influence on the management of your diabetes. The internal dialog that you carry on with yourself plays a key role in how you feel and act. That is why when it comes to controlling your diabetes, via your diet and physical activity, it is important that you remain positive

and focused. So quieten that snide, belittling voice inside you. Be proud of who you are and how much you are capable of accomplishing. Dismiss the accusations that you aren't good enough or strong enough to reach your goals. By paying heed to those negative whisperings, you are simply setting yourself up to fail.

Whenever you catch yourself harboring such negative thoughts, take a deep breath. When you stop being so hard on yourself, it becomes easier to embrace a more positive state of mind and focus on all the good you have accomplished. Just by picking up *The Ultimate Guide*, you have already demonstrated a desire to improve your situation. Of course, it is only one tiny step, but by choosing to learn everything you can about diabetes, you are casting a bright light into the darkness that eats away at you.

One of the best ways to help you turn your attitude around is by keeping a journal. By documenting the food you eat, the amount of exercise and sleep you get daily, as well as your thoughts and opinions, you can start to chart your ascent towards a

more positive future. In this way, not only will you have a record of your successes, it will provide you with an opportunity to reflect on your diabetes fears and anxieties. At the same time, your attention and focus will begin to zero in on how you are improving your circumstances.

In closing, here are eight tips that will help you rise towards the healthy person you are intended to be.

1. Remember, you are not alone. Millions of Americans are dealing with the same condition.

2. Learn as much as you can about the predicament. Knowledge is power especially when it comes to your blood sugar.

3. The accumulation of small gains leads to a positive payoff. Keep in mind that to change your blood sugar issues, you need to unlearn a lifetime of bad habits and that type of behavior modification takes time and requires patience and perseverance.

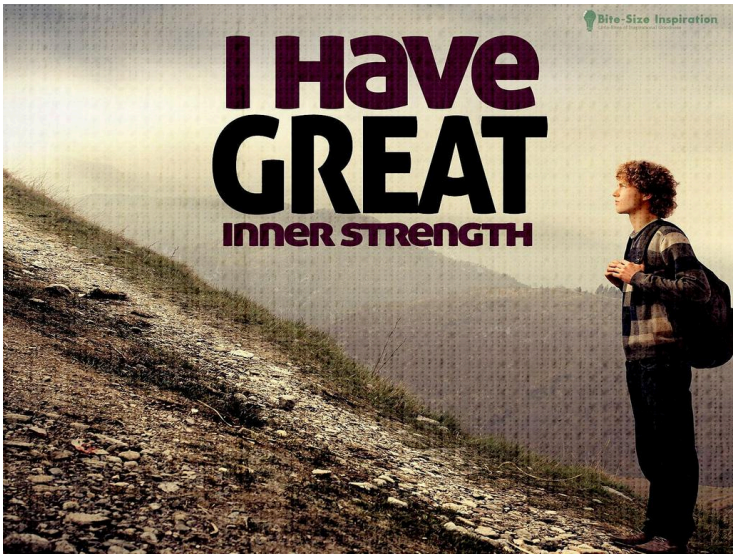
4. Team up with a doctor. Diabetes is a lot easier to deal with when you have a compassionate health care advisor to assist you with the ups and downs of the disease.

5. Enroll in a diabetes education course. Many hospitals offer patients with programs designed to help you better deal with the disease. You'll be grateful that you did.

6. Join a support group. The fellowship of other diabetics will empower you and provide you with positive support.

7. Begin exercising. Nothing helps you get a handle on your diabetes like working out.

8. Keep a journal. Tracking what you eat and how much exercise is an excellent way to get an improved perspective on your blood sugar issues.



So, once you make the decision to take charge of the mental habits that determine the way you live your life, congratulate yourself for embracing such a positive, life-affirming attitude. The emotional benefits generated by such hopeful feelings will reinforce your commitment and give you the certainty that you can continue with your new lifestyle without fear or regret.