

Gestational Diabetes

Gestational diabetes is a medical condition that causes blood sugar levels to become abnormally high, which manifests for the first-time during pregnancy and typically disappears immediately after birth for around ninety percent of affected women. While many women with the condition do not experience any noticeable symptoms, some may experience increased thirst and urination. Although gestational diabetes is treatable, if left unmanaged, the resulting fetus is more likely to have elevated risks of increased birth weight, birth injuries, low blood sugar, stillbirth, and later development of type 2 diabetes. The International Diabetes Federation estimates that worldwide in 2019, gestational diabetes affected one in six pregnant women, with many cases occurring in women living in low and middle-income countries. Despite the prevalence and risks associated with gestational diabetes, as of 2020, researchers have yet to reach a unified consensus on the best guidelines for diagnosis and treatment.

Although evidence of non-gestational diabetes dates back to 1500 BC, there was no evidence or documentation of gestational diabetes until the early 1800s. In 1824, Heinrich Bennewitz, a medical doctor who worked in Berlin, Germany, was one of the first physicians to record and publish a case of gestational diabetes. Bennewitz was caring for a twenty-two-year-old woman during her fifth pregnancy, who according to Bennewitz, suffered from unquenchable thirst and cloudy, stale-smelling urine. When it came time to give birth, Bennewitz and another doctor who specialized in childbirth helped deliver the fetus. Bennewitz described the neonate as being Herculean, with a weight of twelve pounds, and that the birthing process ultimately ended in stillbirth. Bennewitz's case report and description of the woman's symptoms correlated with modern understandings of gestational diabetes. Although people with gestational diabetes oftentimes do not exhibit symptoms, they sometimes suffer from increased thirst like the woman in the case report. Urination increases when the kidneys cannot keep up with filtering glucose, causing the body to excrete excess sugar into the urine. The expulsion of urine pulls away fluids from other tissues in the body, leaving the individual feeling dehydrated and thirsty.

In the late 1800s, James Matthews Duncan, a physician from Scotland, helped to further establish gestational diabetes with clinical observations that continue to hold true in the twenty-first century. Duncan learned from James Young Simpson, who was a prominent professor of midwifery, or the occupation of helping women during childbirth, at the University of Edinburgh, Scotland, in Edinburgh, Scotland. After completing his apprenticeship with Simpson, Duncan continued studying pregnancy and childbirth in London, England. In 1882, he monitored and observed the pregnancies of sixteen diabetic women and came to the conclusion that women can develop diabetes during pregnancy, but that it can go away once the pregnancy is over. Duncan also concluded that women who develop diabetes during pregnancy might be at higher risk of developing the condition again later in life. After publishing his findings in the journal *Transactions of the Obstetrical Society of London* in 1882, Duncan became one of the first people to publish clinical findings on gestational diabetes.

Before the mid to late 1900s, doctors could only screen women for gestational diabetes by determining a patient's medical history and assessing their risks, using a classification system developed by Priscilla White. White was a physician who began her career working at the Joslin Diabetes Center in Boston, Massachusetts, in 1924, which was around the same time that researchers discovered insulin. A normally functioning pancreas produces insulin to regulate blood sugar levels. Diabetics struggle to regulate their blood sugar, either because they cannot produce enough insulin, or because their bodies are resistant to insulin, as is the case for gestational diabetics. White created a classification system that not only helped physicians distinguish between gestational diabetes

and diabetes that exists before pregnancy, but categorized those women according to their age, disease duration, and other health factors. Many physicians adopted that classification system because it helped them more accurately predict pregnancy complications for each gestational and non-gestational diabetic patient, resulting in more tailored treatment plans and better health outcomes for both the fetus and pregnant woman.

Screening methodology shifted away from only obtaining a patient history when, in 1964 in Boston, Massachusetts, John O'Sullivan and Claire Mahan invented the two-step oral glucose tolerance test, which physicians still commonly use as of 2020 to diagnose women with gestational diabetes. In the first step, the patient ingests 50 g of glucose, typically in the form of a solution, and waits one hour before having a technician test her blood glucose value. If that value is elevated, the patient undergoes the second step of the test. During the second step, a healthcare provider gives the woman a 100 g glucose tolerance test that lasts three hours instead of one. If the patient's blood glucose value is elevated again, her physician will diagnose her with gestational diabetes. O'Sullivan, a physician, and Mahan, a statistician, worked together to establish the cut-off blood glucose values for diagnosis, later known as the O'Sullivan criteria. Although many organizations, such as the American Diabetes Association, adopted the O'Sullivan criteria, other researchers suggested that the cutoff values assigned to blood sugar levels in the test only accounted for the pregnant woman's risk of developing long-term diabetes, and did not consider any risk to the fetus.

Disagreement within the medical community on the best ways to screen and diagnose gestational diabetes continued throughout the rest of the twentieth century. Between 1979 and 2005, leading medical professionals organized five international workshops to assess the strengths and weaknesses of gestational diabetes care. Norbert Freinkel, a physician and former president of the American Diabetes Association, organized the first international workshop which occurred in Chicago, Illinois, in October of 1979. During that workshop, participating medical leaders decided that physicians should screen all pregnant women for gestational diabetes between weeks twenty-four and twenty-eight of gestation, which is the time pregnant women are most likely to develop the condition. In the second and third workshops, held in 1984 and 1990 respectively, leaders agreed that patients with gestational diabetes should be encouraged to engage in moderate physical activities, and should undergo a glucose tolerance test at their first follow-up appointment after delivery. The fourth workshop, held in 1997, focused primarily on improving screening methods for women who had a low risk of developing the condition, while the fifth workshop, held in 2005, reviewed new information relating to management strategies and long-term complications.

Despite the frequency of international workshops, as of 2020, the medical community has not reached a universal consensus on effective parameters for diagnosing gestational diabetes. Many medical organizations differ to an extent with their recommendations. For example, the National Institutes of Health recommends the two-step oral glucose tolerance test, whereas the International Association of Diabetes and Pregnancy Study Groups advocate for a one-step test. Critics of the one-step test argue that when healthcare professionals diagnose a woman with gestational diabetes after only one abnormal value instead of two as seen in the two-step glucose tolerance test, more pregnancies become unnecessarily medicalized and a greater burden is placed on the healthcare system. However, supporters of the one-step approach argue that it is more cost-effective and provides better neonatal outcomes. According to the American Diabetes Association, there is evidence supporting both approaches, but they note that more long-term studies are needed to establish a universal approach for diagnosing gestational diabetes.

As of 2020, doctors know that some women are more likely than others to develop gestational diabetes, and those who do develop the condition may exhibit certain symptoms to indicate their diagnosis. Although it is possible for women without any risk factors to develop gestational diabetes, women who are overweight or obese have a higher risk of developing the condition. Women who have previously had gestational diabetes or have a family history of diabetes are also at greater risk, in addition to women who have polycystic ovarian syndrome, or PCOS. Women with PCOS experience symptoms such as small fluid-filled sacs develop in the ovaries, increased testosterone levels, and elevated risks for high blood pressure, heart disease, and type 2 diabetes. Many women who end up developing gestational diabetes do not have any noticeable symptoms. However, some women may complain of increased thirst and more frequent urination.

If left untreated, gestational diabetes can result in complications for both pregnant women and their fetuses. Women with gestational diabetes have a five to seven-fold increased risk of developing type 2 diabetes, a type of diabetes where cells become less responsive to insulin, later in life. They are also more likely to develop gestational diabetes in future pregnancies. As for the fetuses, possible complications include excessive birth weight, birth injury, low blood sugar, and stillbirth. A fetus receives its nutrients directly from the blood of its gestational carrier. If the carrier's blood sugar is too high, the fetus may store extra sugar as fat while also enabling it to grow to an excessive birth weight defined as nine pounds or heavier. During labor, large fetuses are more likely to become wedged in the birth canal, which can cause injury to the fetus and require emergency surgical delivery.

Immediately following delivery, the neonate might experience low blood sugar. In typical gestation, a fetus needs high levels of insulin to process any extra sugar coming from its gestational carrier and can continue to have high insulin levels after birth despite no longer having the carrier's excess sugar. High levels of insulin without elevated levels of blood glucose can cause the insulin to lower blood sugar unnecessarily, which can cause unanticipated low blood sugar. Researchers also state that neonates exposed to gestational diabetes while in the womb experience a higher risk of eventually developing type 2 diabetes. Elevated blood sugar can cause systemic damage, and researchers have suggested that stillbirths may be a result of gestational diabetes. High blood sugar levels can cause damage to blood vessels, and researchers suspect that damage to small blood vessels and poor blood circulation within the womb can lead to stillbirth.

Although there are some studies with conflicting results, many researchers concur that neonates born from women with gestational diabetes may experience long-term negative effects. According to the International Diabetes Federation, those children may be at a higher risk of eventually becoming overweight or obese, or developing type 2 diabetes and high blood pressure later in life. However, some researchers have contested whether those risks are directly caused by gestational diabetes instead of factors like maternal weight and lifestyle habits.

Physicians generally recommend that pregnant women undertake important lifestyle changes to avoid or reduce their risks of developing gestational diabetes. Because diet can drastically impact overall blood sugar levels, physicians may refer women to see a registered dietitian who can create personalized diet plans. They also may recommend exercise at a moderate intensity, as exercise has been shown to lower blood sugar. Women who are at risk of or have already developed gestational diabetes may need to check their blood sugar many times per day using a home blood glucose test kit. If diet and exercise fail to keep blood sugar levels within the normal range, which may happen for ten to twenty percent of women with gestational diabetes, doctors may prescribe insulin injections or oral medication to help control the elevated blood sugar levels. After pregnancy is over, doctors may continue to monitor the women's blood sugar levels for six to twelve weeks to ensure that the values return to a normal range. Because those who are overweight or obese are at a higher risk for developing gestational diabetes, prevention techniques often center around similar strategies of healthy eating and moderate intensity exercise.

While researchers are not aware why some women develop gestational diabetes while others do not, as of 2020 there is some evidence that may support possible causes of gestational diabetes. The placenta, an organ that develops during pregnancy to nourish a growing fetus, produces many hormones to maintain the pregnancy. Some of those hormones can exhibit a blocking effect on insulin, and as the placenta grows and produces larger amounts of those hormones, the risk of insulin resistance also increases. Usually, the woman's body produces extra insulin to overcome resistance. If that extra insulin is not enough to lower blood sugar into a healthy range, the pregnant woman may develop gestational diabetes. The scientific community refers to that process as the contra-insulin effect, which normally starts twenty to twenty-four weeks into gestation, and is why many testing protocols indicate that the optimal time to undergo an oral glucose tolerance test is between those gestational weeks. Researchers also state that during some women's pregnancies, due to increased fat storage, increased calorie intake, and decreased physical activity, blood sugar levels can rise above normal levels and lead to gestational diabetes.

According to the International Diabetes Federation, researchers predict the number of women experiencing gestational diabetes will increase as the overall number of women with diabetes increases.

In 2019, there were an estimated 223 million women living with diabetes, and that number is expected to surpass 343 million women by 2045. As the frequency of diabetes increases, the prevalence of gestational diabetes continues to increase, with hyperglycemia occurring during delivery affecting approximately one in six pregnancies as of 2019.

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