

Diabetes

What is Diabetes?

Diabetes stands for excessive urination (Greek for *siphon*).

- Diabetes Mellitus - High blood sugar (glucose), resulting in a lot of sugar in the urine (mellitus), leading to excessive urination. People usually refer to this as "**Diabetes**". Diabetes results from either absolute deficiency of **insulin**, or due to a relative deficiency in the face of resistance to insulin actions.
- Diabetes Insipidus - The brain cannot produce antidiuretic hormone (ADH), a substance that is responsible for concentrating the urine, or the kidney cannot respond to ADH. The urine of such people is very dilute, appearing like water.

Both conditions are treated in the Division of Endocrinology and Diabetes. **We will limit this section to the different forms of Diabetes Mellitus** (from hereon called "**diabetes**").

What is Insulin?

Insulin is a hormone secreted into the blood stream from the pancreas, an organ situated behind the stomach. Insulin is central to the metabolism of sugars, proteins and fats. Following each meal, carbohydrates are digested and broken into **glucose** and other simple sugars, which are absorbed from the gut into the blood. Insulin is secreted from the **beta cells** in the pancreas in response to a rise in blood glucose, following each meal. Insulin is the key that enables glucose to enter cells in muscle and other tissues, which use glucose as their major fuel source.

What if the body lacks insulin?

Without insulin, sugar (glucose) levels in the blood are very high, as it cannot enter cells, and instead large amounts of sugar are being spilled in the urine. This causes excessive urination and thirst. In spite of excess sugar in the blood stream, the cells feel "starved", and the body starts using alternate fuel sources, breaking muscle and fat. This leads to weight loss, fatigue and weakness, in spite of increased appetite.

Types of Diabetes

There are two major forms of diabetes, now called **type 1 diabetes** and **type 2 diabetes**. Unfortunately, they have been called by many different and misleading names, namely:

Type 1 = insulin-dependent diabetes mellitus (**IDDM**), or juvenile onset diabetes

Type 2 = non-insulin dependent diabetes mellitus (**NIDDM**), or adult onset diabetes

Type 1 diabetes is still the most common type of diabetes in children. However, with the rise in childhood obesity and inactivity, we now observe a growing number of children and particularly adolescents with **type 2 diabetes**, especially in Latinos, Native Americans, and African Americans. There are also other, less common forms of diabetes, associated with specific genetic defects (MODY) or other conditions such as cystic fibrosis, medications, or infection and inflammation of the pancreas (pancreatitis).

Type 1 Diabetes

In type 1 diabetes there is gradual destruction of the beta cells in the pancreas, happening over a few years (or sometimes over a few months, as happens in infants and toddlers). The cause for the destruction is the body's own immune system attacking itself (autoimmune disease), and in this case, the insulin-producing beta cells in the pancreas. There are immune cells that destroy the beta cells and others that produce antibodies that can be detected in a blood test. Type 1 diabetes may also be associated with other autoimmune diseases, most commonly affecting the thyroid gland, that present before, at, or after the diagnosis of type 1 diabetes.

Because of the destruction and lack of insulin, treatment of children with type 1 diabetes relies on giving them back insulin. At present, insulin is given as multiple daily injections with a very thin and short needle or a pump that delivers insulin under the skin through a plastic tube. Other types of insulin, such as inhaled or oral insulin, may in the future replace injections to some degree.

Eventually, after 80% or more of the insulin-producing beta cells are destroyed, there is true insulin deficiency, leading to the typical symptoms of diabetes, which usually appear over a short time (weeks), and become progressively worse:

- Excessive urination (sweet urine, thus diabetes mellitus)
- Bed-wetting in a child who was previously toilet trained
- Excessive thirst and/or dry mouth
- Increased appetite
- Weight loss, despite over-eating
- Fatigue and weakness
- Blurred vision that fluctuates (due to changes in blood sugar)
- Other non-specific complaints are irritability, apathy, decline in school performance and restlessness. Adolescent girls may develop yeast infections

Children often present during an acute illness, such as diarrhea or a "cold", in which case the symptoms of diabetes can develop over days. In addition children may become significantly dehydrated. During an infection and stress there is a higher demand from the body to produce insulin, and the load becomes excessive for the small number of remaining beta cells. Children who are diagnosed during an acute illness are often sicker and develop a condition called **diabetic ketoacidosis (DKA)**. Symptoms associated with DKA, such as nausea or vomiting can be confused with "stomach flu", and the abdominal pains seen in DKA can sometimes lead to a false diagnosis of appendicitis.

What is DKA, and is it dangerous?

As the body cannot use glucose, fat is broken down and **ketone bodies** are produced, resulting in acidosis. These can also be detected in the urine. As more ketone bodies are produced and acidosis progresses, it reaches a dangerous condition called **ketoacidosis**. The child tries to compensate by breathing heavily, and parents may notice their child's breath smells fruity. Other complaints can be nausea, vomiting or abdominal pains.

If left uncared for, diabetic ketoacidosis (DKA) is a life-threatening condition!

Children need to be admitted promptly to a hospital, often to an intensive care unit, that allows close monitoring and support of fluids and electrolyte imbalance, as well as being on the alert for mental status changes. Rady Children's Hospital offers experienced pediatric endocrinologists well versed in administering continuous insulin drips, and an excellent intensive care setting, to treat this serious condition, which can lead to brain swelling.

As in many conditions in pediatrics, prevention is the best strategy. Recognizing the signs and symptoms of diabetes early, can prevent a child from progressing to DKA.

Type 2 Diabetes

Adult onset diabetes was a fair description of type 2 diabetes, up until two decades ago, but no longer. In the United States, increasing numbers of adolescents are now diagnosed with type 2 diabetes, most of whom are obese. Furthermore, type 2 diabetes is also diagnosed more frequently in young adults who are in their 20's and 30's, as compared to a decade or two ago. We know that healthier eating and daily exercise and activity can prevent or delay the onset of type 2 diabetes, in adult people who are at high risk of developing type 2 diabetes.

Most people diagnosed with type 2 diabetes still have normal or elevated levels of insulin. However, they can no longer produce enough insulin to overcome their body's resistance to insulin action. Insulin resistance is commonly observed in obesity, and is exacerbated by inactivity. There is also a genetic component to it, such that African Americans are usually more insulin resistant than Caucasians of equal size. Unlike type 1 diabetes, patients diagnosed with type 2 diabetes have a relative deficiency of insulin. If the child is sick at the time of diagnosis, and/or has very high blood sugar levels associated with marked symptoms such as weight loss, or excessive urination, **insulin** therapy will be started first.

Another reason to start insulin in such instance is that not every child who is overweight or obese necessarily has type 2 diabetes. Therefore, the doctors may need to run some tests to verify that the child does not have type 1 diabetes. For a child or adolescent who is not sick and has few symptoms of diabetes, **diet and exercise** may be the first choice. However, if the symptoms are more pronounced, or if diet and exercise alone fail, treatment with **oral drugs** that either enhance insulin secretion (sulfonylureas, for example Glyburide, Glucotrol, Amaryl), and/or drugs that reduce insulin resistance (Actos, Avandia) and/or glucose production (Metformin), are very effective.

In children with type 2 diabetes, the most common drug used first is **metformin**, which is usually not associated with weight gain or low blood sugars, and is well tolerated. Sulfonylureas, which can cause low blood sugars, are often used as well, usually if metformin alone is insufficient. However, some patients with type 2 diabetes may gradually progress and have low insulin secretion, and require insulin. For that reason, the name non-insulin dependent diabetes is not always accurate, and was replaced with type 2 diabetes.

Gestational Diabetes

Diabetes that develops during pregnancy, usually in the last part of pregnancy, occurs in 1 out of 200 child bearing age women. This is due to the insulin resistance typical of pregnancy. After delivery, most women have normal blood sugar levels again. Up to half of

women with gestational diabetes may develop type 2 diabetes within the next 10 years. Others may have a genetic form of diabetes called MODY (see below), which can present for the first time during pregnancy.

Other types of Diabetes

There are also **less common types of diabetes**, which may warrant different approach and treatment. Children who are misclassified may be subjected to daily insulin injections, instead of pills that would treat them well. Therefore, we make every effort in our Diabetes Center to thoroughly evaluate the cause of diabetes in each child.

- One such “uncommon” type of diabetes is Maturity Onset Diabetes of Youth (**MODY**), a genetic form passed from one generation to the next that affects the ability of the pancreas to secrete insulin. MODY is made up of 5 or more distinct forms, and represents up to 5% of children who may have been classified before as type 2 diabetes.
- Diabetes associated with rare genetic syndromes, mitochondrial diseases, or rare conditions such as Cushing’s syndrome (excess production of steroids by the adrenal glands) or excess growth hormone
- Diabetes secondary to medications (for example, steroids or cancer drugs) or other conditions that destroy or damage the pancreas (for example, pancreatitis or cystic fibrosis), or following surgery to remove the pancreas.

Who gets diabetes in childhood?

Type 1 diabetes

Most of the time there is no prior family member with type 1 diabetes, although other family members may have another autoimmune condition affecting the thyroid, skin (vitiligo) or other organs. Diabetes is NOT contagious !

- There is a 1 in 20 chance of another family member getting type 1 diabetes
- If a first-degree relative of a child has type 1 diabetes, there is a 1 in 10 risk for that child to develop type 1 diabetes.
- If one twin has type 1 diabetes, there is a 50% or greater chance that his identical twins will develop it later in life, sometimes only as an adult.

Type 2 diabetes

In families where there are other members with type 2 diabetes or history of gestational (during pregnancy) diabetes, other members are very likely to develop type 2 diabetes, particularly if they become overweight and obese, and are sedentary. Lack of exercise contributes to weight gain, and insulin resistance, and increase the risk for diabetes greatly.

- **Ethnicity** is an important factor. The risk for type 2 diabetes is higher in Native American, African American, Pacific Islanders, and Hispanics, compared with non-Hispanic Caucasians. In some populations, living a Western society lifestyle, the risk of developing type 2 diabetes for an individual who has a first degree relative with diabetes, is 50% or even higher.
- **Low Birth Weight** under 5 ½ lbs for a full term baby, or **Large Birth Weight** of 10 lbs or over, or being born to a **mother with diabetes** during pregnancy, are all associated with higher risk of type 2 diabetes.
- **Obesity** is a major risk factor for developing type 2 diabetes, even without family history of diabetes. In some populations, even a modest weight gain of 20 lbs can result in type 2 diabetes.

Your child was just diagnosed with type 1 diabetes, and was discharged from the hospital. What to expect ?

1. Clinic visit schedule

First visit: 7-10 days after discharge. Making sure all is well with the diabetes management and adjustment, prescriptions are fine, examine the child, and to answer any questions or concerns.

Second visit: 1 months following initial visit. Often the child is in or entering the honeymoon period, and adjustments and further education is needed

Subsequent visits: every 3 months. Sooner if there are problems

In each visit a resident/fellow physician in training may see the child first, prior to the attending physician.

A nurse, social worker and dietitian are available. Separate outpatient meetings with the dietitian or nurse alone are possible to book

2. Contact with the diabetes team

Urgent matters - call "doctor on call" when:

- Child is sick and has high blood sugars persistently over 30
- Vomiting, having diarrhea or not eating well
- Has moderate or large urine ketones
- Low blood sugar less than 40, seizure or requiring assistance

Whenever sick, always check for ketones, even if normal blood sugars.

Contact doctor on call at:

- 858-966-4032 [8AM-4:30PM Mon-Fri]
- 858-576-1700, press zero, then ask for endocrine doctor on call [After hours, weekends, holidays]

Non-urgent matters:

- Child is about to run out of prescription
- Making routine insulin adjustments, or plans for upcoming events
- School forms
- Reviewing lab results
- Scheduling a meeting with a nurse or dietitian

Call office during routine hours: (858) 966-4032, ask to speak with nurse, or dietitian. Response is within 24 hours.

Families are encouraged to fax school forms, request for supplies, or blood sugar and insulin dose records to our office: Fax (858) 966-6227

3. The honeymoon period. What is it?

A few weeks following the diagnosis of type 1 diabetes, insulin doses are lowered, while maintaining excellent blood sugar levels.

Is the diabetes going away? No!

This is the honeymoon period, a period of excellent control, with very low insulin requirements. A few children may even be able to skip at least one insulin injection. The honeymoon period may last from a few months and up to a year or longer, depending on the amount of insulin-producing beta cells left in the pancreas. Therefore, children who are diagnosed early are less sick and without DKA usually have a longer honeymoon period.

High blood sugar levels that are present prior to diagnosis are toxic to the remaining beta cells, and prevent those cells from producing insulin effectively. Once insulin injections bring down the blood sugar levels and give the remaining beta cells some rest, those beta cells return to function. The beta cells are able to help-out by secreting insulin whenever there is a need, allowing for lower insulin doses. It takes a few weeks to enter the honeymoon period because initially most children eat a lot in order to regain their lost weight and strength, and the remaining beta cells have not yet recovered. Unfortunately, the autoimmune process continues to gradually destroy the remainder of beta cells. When there are hardly any beta cells left, the honeymoon period ends. It ends gradually, marked by gradual increase in insulin requirements. Keeping active and avoiding excessive weight gain may help reduce the demand for insulin, and prolong this period for a bit longer. Prior attempts to manipulate the immune system and prolong the honeymoon period have not been useful. There are research trials addressing this that are currently ongoing, and those can be discussed with our physicians.

Goals of treatment at the Diabetes Center, and what is done

1. Maintain blood glucose levels (and **A1c**) as close to normal, while avoiding low blood glucose levels (hypoglycemia). This requires frequent blood sugar checks, at least 4 times daily in patients on insulin, before meals and at bedtime. Better control of blood sugar levels results in less long-term complication and slower progression of complications, should they develop.

Hemoglobin A1c is a blood test done from a finger stick every 3 months, which measures the average blood glucose levels over that time, and helps guide therapy and home blood glucose monitoring. Continuous glucose monitoring is now also available

2. Diabetes to revolve around a child's life, and not visa versa. Towards that goal, a qualified and experienced diabetes team is available to constantly tailor the treatment plan (insulin regimen and diet) to the individual's needs. These revolve around the daily schedule, meals, and family needs. To address these issues, our team includes certified diabetes educators, nurses, dietitian, social worker and physicians giving 24-7 coverage. **Good communication and education are key to good outcomes**

An **insulin pump** is a useful tool to achieve some goals, but requires responsibility and a dedicated effort in managing diabetes. In addition, certain basic skills need to be learned before a pump can be prescribed. Good preparation is the key to success in the dozens of patients who are doing great with the insulin pump. We use 3 major brands of insulin pumps, and the ultimate choice of which pump to use is individual.

3. Promote healthy weight and diet. This is important in controlling blood pressures and lipid levels such as cholesterol and triglycerides. Preventing further weight gain or advocating moderate weight loss in obese patients with type 2 diabetes often helps control blood sugars, and prevents other complications associated with obesity.
4. Monitor for complications and other conditions associated with diabetes, during each visit to the clinic, and through periodic labs. These include:
 - Height and weight to monitor growth. Growth can be affected by diabetes, or conditions associated with diabetes: abnormal thyroid or adrenal glands, or celiac disease
 - Blood pressure checks at each visit. Hypertension is particularly harmful in diabetes, and advances other complications more rapidly.
 - Monitor the thyroid gland on exam, and yearly thyroid blood tests.
 - Monitor urine for protein leak (urine microalbumin), as a sign of kidney complication due to diabetes. If left untreated this can lead to kidney failure and dialysis in adulthood.
 - Ensure dilated eye examination done yearly after 5 years duration or as needed. This is to monitor for diabetes damage to the small blood vessels at the back of the eye, which can lead to blindness if left untreated
 - Ensure good foot care and sensation, building good habits for adulthood. Preventing ingrown toenails and infections
 - Monitor lipid levels (cholesterol, LDL, HDL and triglycerides), especially in type 2 diabetes, and treat as needed. This is crucial since abnormal lipids results in earlier heart disease and infarcts.