Not every form of diabetes is **the same**

Dividing diabetes into type 1 and type 2 is relatively common. "But few people know that other types exist, including monogenic diabetes, which is caused by carrying a mutation of a certain gene," explains Štěpánka Průhová, who is involved in research into this hereditary disease.

There are approximately one million diabetics in the Czech Republic. The vast majority of them face type 2 diabetes in adulthood and many fewer, type 1, which is inherited polygenically. But less than 5 percent of patients have a somewhat different disease, one that is autosomally inherited, so patients hand it down in families and it is caused by a pathogenic variant in one of the genes. It is called monogenic diabetes mellitus.

"If diabetes occurs in a young person, whether a child or an adult under the age of 40, who is thin and has negative autoantibodies, it can be assumed that it's not type 1 diabetes. If they're not obese, it's not likely to be type 2 diabetes either. In these cases, we begin to address whether their parents or grandparents were treated for diabetes. If it is shown that there have been several generations in the family where diabetes has manifested itself early, the patient is indicated for genetic examination," says Associate Professor Štěpánka Průhová, describing cases where doctors consider the genetically dependent variant of diabetes.

If monogenic diabetes is detected in patients, a different treatment can be applied than in type 1 and type 2 diabetes. However, the procedure chosen depends especially on the genetic background detected and extent of the disease. Glucokinase diabetes is a mild variant of the disease. "While the patient meets the criteria of diabetes according to the Diabetes Society and should start treatment according to current guidelines, these people have been found to have a disorder that has been present since birth, and will continue until old age. Fortunately, these patients tend not to develop the chronic diabetes complications we're most concerned about. Therefore, there's no need to start treatment because slightly elevated blood glucose fluctuates only minimally and does not increase over time, as we know with other types of diabetes. Children with this diagnosis can play sports, don't have to inject insulin, and don't even have to adhere to a strict diet. They only have to slightly reduce their intake of fast sugars in food, such as giving up sweetened soft drinks. It tends to be very good news for parents, which is why we call this variant 'good diabetes'", Associate Professor Průhová explains.

But hereditary forms of diabetes can be significantly worse. If a patient has another type of disease (such as changes in the HNF genes) and at the same time does not cooperate properly with doctors and does not take their medication, there is a high risk of complications and a need to apply intensive treatment, sometimes including insulin. For cooperating patients, it is possible to try treatment with oral antidiabetics, specifically sulfonylurea derivatives, which they often respond to better than if they were to receive insulin. According to studies, up to 70 % of people with MODY (maturity onset diabetes of the young) – as this type of diabetes is also called on the basis of clinical observation – can replace insulin treatment by treatment with tablets, which most patients welcome, especially children.

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We can't fix genes

Doctors today mainly focus on improving the diagnosis of the disease. As Associate Professor Průhová states, thanks to next generation sequencing methods it is possible to analyse multiple genes in one examination. "That's why we've developed a panel of hereditary diabetes genes so that we can investigate all the genes that are known in relation to diabetes at once."

But experts have thus far not been able to repair mutated genes. "If I were to work from other model diseases where certain vectors can be inserted or a specific area of a gene can be repaired, it would potentially be possible. But the responsible genes work throughout the body, and so far I can't imagine a way we'd be able to repair them all. The question is also whether it makes sense at all for less severe forms of the disease," Štěpánká Průhová says, admitting that development in the treatment of diabetes is directed toward the majority types rather than to rare cases. "But patients with MODY also benefit from this because we can choose the medicine that's the most suitable for them. Sometimes we use drugs designed for something else and find out that they work beautifully, especially for some of these other types of diabetes. A perfect knowledge of the etiology of diabetes helps tremendously."

Knowledge of genetics is also useful elsewhere

Associate Professor Štěpánká Průhová is very active in the field of scientific research. Aside from being in charge of 120 paediatric patients with type 1 diabetes at Motol Hospital, she is involved in several research projects. She uses her knowledge of genetics in paediatric endocrinology as well, where she deals with growth disorders and uses genetic research to figure out what causes a given problem. "There are two major projects underway at the moment that are tasked with finding out how genetic causes influence body height in specific families. We are investigating what makes a person shorter or taller, and what subsequently influences their growth during childhood and adolescence," she explains.

Associate Professor Štěpánka Průhová chose hereditary forms of diabetes and their causes as the topic of her postgraduate study at the Third Faculty of Medicine. In addition to her care for diabetic patients at the Paediatric Clinic of the Second Faculty of Medicine and Motol University Hospital, she works in the Laboratory of Molecular Genetics, where she performs molecular genetics diagnostics of MODY diabetes and some forms of neonatal diabetes. She is the vice-dean for doctoral studies and foreign affairs at the Second Faculty of Medicine at Charles University.