A **cure** for diabetes is not on the horizon yet

Almost a hundred years ago, a diagnosis of diabetes mellitus was a death sentence. The discovery of insulin, however, was a breakthrough: for the first time, it was possible to successfully treat the fatal disease. In his research, paediatric diabetologist Zdeněk Šumník examines risk factors that lead to the development of type 1 diabetes.

Can it be predicted whether a child will get diabetes?
I'll answer in a slightly roundabout way. Type 1 diabetes is one of the autoimmune diseases where genetic and environmental factors contribute approximately equally to its onset. We know with a fair amount of detail that genes increase the chance of getting sick and the risk they bring, and we are able to make a kind of genetic prediction. The problem is that the estimate is still relatively inaccurate, because even with the combination of the highest-risk genes, "only" one in five will get sick.

On the other hand, we still know relatively little about external environmental factors and their role in the diabetogenic process. This is due, among other things, to the fact that in the shortest case, a clinical manifestation of diabetes with a typical rise in blood glucose takes place several months after the onset of the autoimmune process. However, this is measured in years or decades. According to the current thinking, environmental factors are responsible for the primary activation of the immune response, which – after a certain time – leads to the destruction of beta cells on the islets of Langerhans. It's not yet clear whether the preclinical phase of the disease occurs autonomously without additional external impulses or in certain waves of attenuation and reactivation.

This implies that in order to reasonably estimate the lifelong risk of developing type 1 diabetes, we would need to carry out a robust long-term study starting in infancy. With a little luck, they could answer the question of the primary trigger of autoimmune inflammation in the islets of Langerhans. If we were able to identify such a factor, it would theoretically be possible to eliminate or at least supress its actuation for at-risk populations. Some common viruses seem to be the most promising in this regard, even if vaccination against them with the goal of diabetes prevention thus far is something that's off in the distant future. In addition, the preclinical phase of type 1 diabetes begins relatively early, most often by the age of five, which further complicates the technical implementation of studies and possible preventive measures.

If you perform an examination on a child, what information do you share with the parents?
On the basis of a combination of genetic parameters and screening for specific antibodies, we can say with approximately an 80% probability whether diabetes will develop in the next five years. This sounds rather convincing, but it makes sense to perform this examination only in at-risk populations, which means for close relatives of people with diabetes. It cannot be recommended at the level of the entire population due to the still relatively low incidence of type 1 diabetes among children.

If you know that the risk of the disease is high, are you able to prevent its outbreak or at least delay it?
Unfortunately, we don't have such an option at this time, and therefore it doesn't seem rational to expand the diabetes prediction programme beyond clinical trials. A drug with the generic name of teplizumab - an autoantibody acting against one type of lymphocyte – represents a new hope for children in the preclinical period of type 1 diabetes. Only in the case of this drug has it recently been proven that it slows the progression toward clinical diabetes in children by an average of two years. This is a very big breakthrough. Two years without insulin with normal blood glucose values is definitely worth it. We will begin testing this very promising drug in the Czech Republic in the fall. But this doesn't change the fact that at present we can only advise families to monitor the clinical signs of diabetes, which has little to do with real prevention.

Professor Zdeněk Šumník is the head physician at the Paediatric Diabetes Centre of the Paediatric Clinic of the Second Faculty of Medicine and Motol University Hospital. His research interests include the detection of risk factors for the onset of type 1 diabetes and the use of modern technologies for its therapy.

Can't the outbreak of the disease be influenced by an inappropriate diet?
I always wonder in this context whether we truly know what an appropriate diet for our children is, but that would be a slightly different discussion. Of course, in general, the need for insulin depends on body mass index; type 1 diabetes actually breaks out earlier in obese children than in thin children, but we cannot specifically intervene in diet.

Preventive screening in small children may not make sense if you have nothing to offer them yet.
There is no population screening in the Czech Republic, but some states in Germany and Sweden have already gone down this path. They decided to screen children between ages three and five for the presence of autoantibodies and basic risk genes. Nevertheless, this is an initiative at the cutting edge of clinical research – monitoring alone certainly will not improve the health or prognosis of these children. Pharmacoeconomic studies have clearly shown the lack of effectiveness of mass screening for type 1 diabetes, which is why in our environment I do not now consider it rational to talk about it seriously. It would of course be a different situation if effective preventive measures were available – then we would try to find children in the preclinical phase in the child population and enable them to extend their lifetimes without diabetes.

Is there a chance that in the next 10 to 20 years scientists will make a major discovery that will lead to a complete cure of diabetes, so that diabetics will not have to rely on insulin injections their entire lives?
Of course, hope exists. Twenty years is a very long time, but at this point I personally would count myself among the sceptics of a so-called complete cure for type 1 diabetes. Insulin is a hormone necessary for survival, and if it is absent, as is the case with type 1 diabetes, it should ideally be administered to the body in amounts that are as close to the physiological norm possible. One possibility is to create an artificial pancreas using a combination of a continuous blood glucose monitor, insulin pumps and an algorithm that would connect the two devices. In the last few years, research in this field has been truly unprecedented, and the first prototypes have been gradually getting to patients.

However, if you are thinking of constructing fully functional replacement beta cells, that's a much longer road ahead. Despite some success in efforts to reprogram other cells to beta cells, they still haven't managed to achieve an adequate capacity of insulin production capable of fully replacing one's own tissue. Another problem is the increased risk of reactivation of the immune system after the implantation of these cells, and their limited sensitivity to rapid changes in blood sugar levels. I don't see much light at the end of this tunnel, but of course I'd be glad to be wrong.

Are there proposals for treatment solutions that appear at international conferences that you consider too futuristic?
One of these is so-called smart insulin, which would be absorbed from a subcutaneous depot on the basis of current blood glucose. Insulin is naturally produced in the pancreas, gets into the portal vein, can act very quickly in the liver first, then is spread throughout the body in the blood. Insulin applied by pen or pump into the subcutaneous tissue, as is common today, cannot match this sophisticated system in its effectiveness; insulin simply does not belong in subcutaneous tissue. According to the smart insulin creators, a change in the structure of the insulin molecule would be caused by its reactivity to the surrounding glucose concentration. The rate of absorption would increase or decrease as needed. A patient would thus inject insulin, which would then take care of the rest itself. But that seems too futuristic to me.