Follow-up programme for children and teenagers with early-stage Type 1 Diabetes

-Baseline visit-

www.edent1fi.eu

EDENT1FI
European action for the Diagnosis of Early Non-clinical Type 1 diabetes For disease Interception

Dear Parents,

Your child has received a diagnosis of early-stage Type 1 Diabetes (T1D). It is completely natural to feel uncertain and wonder what is coming next and how this is going to affect you and your child's lives. You are not alone, there is a team ready to guide you through this journey!

While you slowly adjust to the news and learn more about T1D, your child has the possibility to participate in a follow-up programme tailored for children and teenagers with early-stage T1D. The follow-up programme aims at determining disease progression and promptly intervene with a therapy, minimizing the risk of complications and providing the best possible care for your child.

What is early-stage T1D?

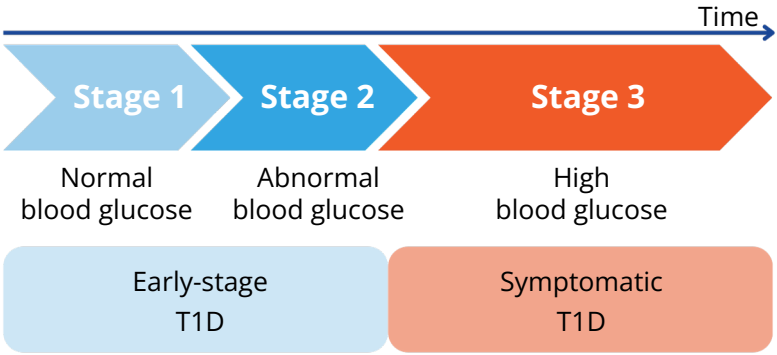
Your child participated in the EDENT1FI T1D autoantibody screening. As a result, we found out that he/she has 2 or more autoantibodies in his/her blood. This means that he/she is in the early-stage of T1D. There are no symptoms associated with this stage: it is a presymptomatic stage.

In early-stage T1D, the immune system mistakenly attacks the insulin-producing cells (called β-cells) of the pancreas. This means that the production of insulin decreases over time until it is no longer produced.

The autoantibodies detected in your child's blood serve as a marker of the ongoing autoimmune process.

The role of insulin is to keep the levels of sugar (glucose) in the blood under control. When glucose is high, insulin brings it down. Imagine insulin as a key that opens the doors of the cells in your body and let glucose flow in. If insulin is absent or too little, the doors of the cells stay closed and glucose remains in the blood.

In early-stage T1D, insulin is still produced but in decreasing amounts or produced in very low levels. Therefore, levels of glucose in the blood can be normal (this is defined as Stage 1 of T1D, as shown in the scheme below) or the



levels can be already altered (Stage 2), but no symptoms are present.

What can my child expect?

Your child can continue to play, do sports, travel, play music and eat as usual. You should not worry too much about changing lifestyle or starting treatments. If you are concerned about this, we are here to support you and answers all your questions. You could also look for patients groups in your city that can give you first hands insights on their experience.

What is Stage 3 T1D?

Stage 3 T1D is the stage of T1D when blood glucose levels are increased. Treatment with insulin might begin at this stage; your doctor will advise you on this. Stage 3 can arise months or even years after the initial diagnosis of early-stage T1D. This stage might be accompanied by signs like:

- fatigue and lack of energy
- weight loss
- frequent urination
- thirst
- signs of dehydration (like dry skin)

These signs can easily be missed and if they are ignored for a long time, a child can become extremely unwell. However, we can prevent this together! Avoiding your child becoming unwell is our priority. This is why we suggest that you enroll your child in the follow-up programme.

What does the follow-up programme entail?

In the follow-up programme, T1D progression is monitored by measuring a number of parameters (like blood glucose level) at certain time points. We call these 'markers of progression'.

Participation in the follow-up programme of EDENT1FI is tailored to your child's estimated speed of disease progression. The latter refers to the risk of developing symptomatic T1D (Stage 3) within the next 2 years.

How is the speed of progression estimated?

The speed of progression to Stage 3 T1D is calculated based on certain markers of progression in your child. Information on these markers are gathered by a doctor or a nurse during a baseline visit at your clinic. During this visit, the doctor or nurse will perform a test called 'Oral Glucose Tolerance Test', during which venous blood is drawn.
The sampled blood will also be used to assess the levels of other markers, like Haemoglobin A1c and IA2 autoantibodies (see Glossary).
These data, together with the age, sex, weight and height of your child, allow us to estimate the speed of progression to

Stage 3 T1D.
Moreover, if you want, a Continuous Glucose Monitoring sensor can be placed on your child's arm (like in the picture below) to monitor glucose levels from home. The sensor might look scary to you, but we can assure that it is not painful!

What is an Oral Glucose Tolerance Test (OGTT) and how should my child prepare for it?

During the OGTT, your child will be asked to drink a sweet, glucose solution.
The doctor withdraws a small volume of venous blood before your child drinks the solution and after. The sampling of the blood after the solution is drank is repeated for seven times in 2 hours.

We ask your child to be fasting for at least 8 hours prior to the OGTT (drinking water is allowed). It is also important that for the 3 days prior to the test, physical exercise is restricted and meals rich in carbohydrate should be avoided. Doing otherwise might affect the result of the OGTT.

What is a Continuous Glucose Monitoring (CGM) sensor?

A CGM sensor continuously (every few minutes) monitors the glucose levels. The CGM patch (picture on the left side) has a thin, flexible filament that when placed under the skin measures the glucose levels. This sensor is connected to your mobile phone *via* Bluetooth and a mobile app records the data. The sensor needs to be replaced every 7 days. The doctor or nurse will train you on how to do it on your own. It is very easy!

Do not worry about showering or swimming, the sensor is water resistant! If by any chance your child needs to undergo a MRI or CT-scan, please notify the responsible doctor that your child is wearing a CGM sensor, as it may need to be removed.

Based on the information gathered during the baseline visit, a progression score is calculated and we can advise you on how often your child should be seen.
We aim to communicate to you the results of the progression score within 2 months from the baseline visit,

after which you will be asked to return to the clinic for a thorough explanation of the follow-up process. We will be available to answers all your questions and solve your concerns.

At the baseline visit and throughout the follow-up, you will be asked to fill in questionnaires to assess the psychological impact of receiving the diagnosis of early-stage T1D and that of following a monitoring programme.

What to do while waiting for the results of the baseline visit

There is nothing you should necessarily do or act upon at this stage. If you like, you can educate yourself on T1D. Be aware that most material you find online refers to symptomatic Stage 3 T1D, which is not the stage in which your child is in right now. Moreover, not all material you find on the internet is trustworthy. If you are in doubt, consult your doctor. To help you, we selected some websites that you can consult to start with (see page 6).

During the baseline visit, you will receive a glucose meter for you to measure blood glucose in your child, by using a drop of blood taken by a finger prick. Use the glucose meter any time your child experiences illness or you see symptoms. The doctor will thoroughly instruct you on how to use the home glucose meter and on how to interpret the output values. Any time you are in doubt, do not hesitate to contact your reference doctor and ask for clarifications.

We know that receiving the diagnosis and envisioning a future with T1D can be a lot to take in. If you feel you need help to process the news, do not hesitate to talk about it with your doctor and seek psychological support. There are also patients support groups that you can connect with and can aid you in navigating this new situation.

Taking part to the follow-up programme will give your child the possibility to promptly access treatments when necessary and avoid the traumatic experience of having diabetes complications.
Our mission is to provide continuous support and education to families to navigate through this new, challenging experience. You are not in this alone!

What happens to the data collected during the EDENT1FI follow-up programme?

The data collected during the study are stored in a secure central data management site at Helmholtz Munich, where also the data of other study sites are stored. Each participant of the EDENT1FI follow-up programme receives a unique identifier (this is a sort of personal code) that is linked to the data, so that your child's name will not be visible. This is to guarantee the privacy of your child when handling the data.

If you have questions regarding the data management, do not hesitate to ask your doctor for additional information. He/she can refer you to someone at EDENT1FI that can answer all your questions about this matter.

Interesting readings

www.edent1fi.eu
The website of EDENT1FI collects information and news on the project, a helpful glossary and much more.

www.diabinfo.de
Website of Helmholtz Munich that gather information on Type 1 and Type 2 Diabetes and evidence-based suggestions on how to live with T1D.

[Insert website of local associations and patients support groups]

Glossary

Autoantibodies

Autoantibodies (such as IA2 autoantibody) are antibodies that your immune system builds against your own insulin-producing cells of the pancreas (β-cells). They are also called *islet antibodies*. Over time, these antibodies destroy the β-cells, leading to insulin deficiency and high blood glucose levels.

β-cells

These are the cells of the pancreas that produce insulin in response to the increasing level of sugar in the blood (for example after a meal).

Continuous Glucose Monitoring (CGM)

In CGM, the blood glucose level is measured every few minutes through a small sensor inserted in the skin of the arm. The sensor transmits the data to an app on your mobile phone that records the measurements. The sensor can also be connected to an insulin pump that can directly inject insulin when the measured glucose concentration in the blood goes above a certain threshold.

Haemoglobin A1c (HbA1c)

HbA1c is a sort of 'blood memory'. Measuring the concentration of HbA1c in the blood reveals the average of blood glucose levels in the previous 8-10 weeks.

Hyperglycemia

Is a condition of high blood glucose that generally occurs when insulin is not produced (or not enough) by your body. This is the case in T1D. Hyperglycemia manifests with symptoms like fatigue, frequent urination, thirst and weight loss. When T1D is not diagnosed or hyperglycemia is not treated, acute complications might occur.

Insulin

Insulin is an hormone produced by the β-cells of the pancreas in response to an increased level of blood glucose, for example after a meal. Insulin is necessary for the cells to 'absorb' the glucose from the blood. Glucose is the main source of energy that the cells of our body use. The cells need energy to carry out their functions. If insulin is not produced, glucose cannot move into the cells and be used. Therefore, it stays in the blood where it accumulates, leading to hyperglycemia.

Glossary

Markers of progression

This is an expression we use to define the set of biological indicators (biomarkers) used to estimate the speed of progression to Stage 3 T1D. These include HbA1c, autoantibodies levels and blood glucose levels.

Oral Glucose Tolerance Test (OGTT)

After drinking a sweet, glucose solution, a small volume of venous blood is drawn (through a cannula inserted on the arm) to measure glucose concentration. Blood is drawn seven times within the 2 hours following the drinking of the glucose solution. Blood is also sampled one time before the solution is drank, to assess the baseline level of blood glucose.

Estimated speed of progression

It is calculated based on age, weight, height and the value of specific markers. It indicates the risk of developing symptomatic Stage 3 T1D within the 2 years following the calculation. The risk can be low, moderate or high.

The role of EDENT1FI

At EDENT1FI, we are working to revolutionize how we tackle T1D in European children. EDENT1FI is a global collaboration between 27 partners in 13 countries from academia, industry and people living with T1D, bringing their knowledge and experience together for one common goal: to inspire trust and arrest T1D at the presymtomatic early-stage. This 5-year Horizon Europe project is coordinated by the team of Prof. Chantal Mathieu of the KU Leuven (Belgium) and co-coordinated by the team of Prof. Anette G. Ziegler from Helmholtz Munich (Germany).

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