



The Natural History Study of Type 1 Diabetes

This handout is designed to provide you with information about *Phase 2* (baseline risk assessment) and *Phase 3* (follow-up risk assessment). (*The technical terms and words shown in **bold** type are defined at the end. The word “you” used in this handout refers to you or your child.*)

Introduction

Relatives of people with type 1 diabetes have a 10 to 15 times greater risk for developing type 1 diabetes than people with no family history. For this reason, TrialNet is screening first, second and third degree relatives of people with type 1 diabetes for **biochemical autoantibodies**. The presence of these autoantibodies, such as GAD65, IAA and ICA512, is a sign that your **immune system** may be attacking the insulin-producing cells (**islet cells**) in your pancreas.

Because you have a relative with type 1 diabetes, you had a blood sample drawn for *Phase 1* (screening) of the Natural History Study. This sample did contain one or more of the biochemical autoantibodies. You also may have had another blood sample drawn to confirm the initial positive test result. These results show that you are more likely to develop type 1 diabetes than most other people, but we still do not know just how likely. Some people with autoantibodies will not develop type 1 diabetes.

Phase 2 – Baseline Risk Assessment

The purpose of this phase is to gain a better understanding of your risk for the development of type 1 diabetes. It will also help us to improve how we determine the risk for developing diabetes. Because several tests will be performed, more information will be available to estimate your risk for developing type 1 diabetes over the next 5 years.

There is a separate informed consent form which you will need to sign for Phase 2.

The tests in Phase 2 will be done after an **overnight fast**. They will require that a needle be placed in a vein (**intravenous line: IV**) before the test begins. All of the blood samples drawn for the tests will be taken through the IV line.

The total time for this visit will be 3-3½ hours (including measurements done such as height, weight and blood pressure).

Blood will be obtained for the following tests: (a description of each test follows this list)

- ◆ **Oral Glucose Tolerance Test (OGTT)**
- ◆ **HLA**

- ◆ **HbA1C**
- ◆ **Biochemical Autoantibodies**
- ◆ **Samples for Storage**

Test Descriptions:

✓ **Oral Glucose Tolerance Test (OGTT):**

This test is used to diagnose diabetes. It measures how much the blood sugar rises and how much insulin the cells (islet cells) in the pancreas release after you drink a sweet liquid. The drink looks and tastes like a soda and contains a lot of sugar. The sweet drink will need to be finished within 5 minutes. Several blood samples will be drawn through the IV line over a two-hour period. The samples will measure the changes in both your blood sugar and insulin levels during the test.

✓ **Human Leukocyte Antigen (HLA):**

HLA is an area on your **chromosomes** (part of DNA) that contains a group of genes. Some people with certain kinds of HLA gene combinations have a higher risk of developing type 1 diabetes. Some people with other types of HLA gene combinations have a lower risk for developing type 1 diabetes.

✓ **Hemoglobin A1C (HbA1C):**

This test will measure your average blood sugar level for the past 3 months.

✓ **Biochemical Autoantibodies (if confirmation sample not drawn previously):**

This test will be done to confirm the biochemical antibodies found in your initial blood sample.

✓ **Blood Samples for Storage:** (These samples will only be drawn at specific study sites)

In the future, the stored blood samples and DNA could be used to learn more about how diabetes develops. Scientists can look at genes that are involved in making proteins. Proteins can be studied to learn how the body's cells behave. Certain proteins may be involved in the development of diseases, specifically type 1 diabetes in this study.

The amount of blood being drawn will be based on your age and weight. In small children, these samples may not be drawn initially. At the end of *Phase 2*, you will be provided with an estimate about your risk for developing type 1 diabetes in the next 5 years.

Your risk may be estimated as:

- ◆ \leq (*less than*) 25%
- ◆ \geq (*greater than*) 25%
- ◆ \geq (*greater than*) 50%

There is still much to be learned about predicting who will develop type 1 diabetes so we cannot tell you for sure if and when you might develop diabetes. This study should help create better ways to predict diabetes.

If the tests listed above do not indicate that you have diabetes, you will be eligible to participate in the next phase of this study.

The next phase after this one is the Follow Up Risk Assessment (Phase 3), *which will begin 6 months after your Phase 2 testing*. The purpose of Phase 3 is to continue to monitor your risk level.

Phase 3 – Follow Up Risk Assessment

This phase will begin 6 months after the testing you had in Phase 2. During this phase, you will be closely watched to see if any tests show that your risk level has changed. You will also be watched closely for the possible development of type 1 diabetes.

There is a separate informed consent form which you will need to sign for Phase 3.

In Phase 3, the tests are done every 6 months for the next 5 years. The tests done in this phase are similar to the ones you had in Phase 2.

Blood will be obtained every 6 months for the following tests (descriptions can be found under Phase 2):

- ✓ Oral Glucose Tolerance Test (OGTT)
- ✓ Hemoglobin A1C (A1C)
- ✓ Biochemical autoantibodies
- ✓ Samples for storage

The results of these follow up tests will be used to help us learn more about risk factors with the development of type 1 diabetes. These results will be used to see if you qualify for other research studies.

The other studies are called prevention trials. They are done to test different kinds of treatments that might help to prevent type 1 diabetes. If you are eligible, you will be told about available prevention trials.

If you develop type 1 diabetes, there may be an opportunity for you to participate in other studies. These studies will test treatments that may help to maintain insulin secretion in people newly diagnosed with type 1 diabetes.

Glossary

◆ Biochemical autoantibody/autoantibodies:

These proteins are made by the immune system of the body. The proteins are usually made when the body comes in contact with a foreign material it doesn't recognize. The purpose of antibodies is usually to protect the body from infections.

In type 1 diabetes, the immune system decides that the islet cells are “foreign” and begins its attack. When these antibodies appear in the blood, it is a sign that the immune system may be attacking the cells in the pancreas by mistake and the risk of type 1 diabetes is increased.

◆ **Blood samples for storage:**

There are many things about the development of type 1 diabetes that are not known. Scientists are discovering new ways to learn about how it develops. Blood samples are stored so these scientists, with permission from TrialNet researchers, can use them to test their theories or new techniques.

◆ **Chromosome(s):**

A substance (containing DNA) found in the center of a cell (nucleus) that contains your genes or hereditary factors.

◆ **Hemoglobin A1C (A1C):**

This test measures your average blood sugar for the past 3 months. A value less than 6 indicates your blood sugar has been in a normal range.

◆ **Human Leukocyte Antigen (HLA):**

This test identifies genes that determine the type of white blood cell markers you have inherited. Some people with certain combinations of these genes have a higher risk of developing type 1 diabetes. Some people with other types of HLA gene combinations have a lower risk for developing type 1 diabetes.

◆ **Immune system:**

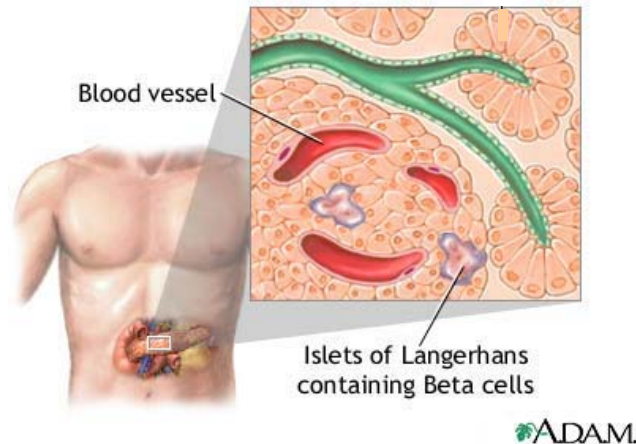
The body’s defense mechanism that is involved in protecting the body against foreign invaders such as bacteria or viruses. Special types of white blood cells are programmed to recognize and attack foreign substances entering the body. Sometimes the immune system makes a mistake and identifies the islet cells in the pancreas as foreign. The immune system then begins to destroy the islet cells, which can eventually result in type 1 diabetes.

◆ **Intravenous line (IV):**

The word ‘intravenous’ means “within a vein”. For the tests in this study, a soft plastic tube (line; catheter) attached to a needle is placed into a vein of your body. Once the line is inserted into the vein, substances can be given through the IV, such as glucose (IVGTT), or blood can be drawn out. Once the test is completed, the IV line will be removed.

◆ **Islet (pronounced ‘eye-let’) cells:**

Islet cells are clusters of specialized cells found scattered throughout the pancreas. These clusters include the cells that make insulin (beta cells).



◆ **Oral Glucose Tolerance Test (OGTT):**

This test measures how much your blood sugar rises after you drink a sweet liquid, and how much insulin your islet cells release to bring the blood sugar (glucose) level back down. This test can be used to diagnose diabetes.

Within a 5-minute period, you will drink a sweet liquid that looks and tastes like soda. Blood samples are then drawn through the IV line over the next two hours. Your glucose and insulin levels will be measured in the blood samples.

◆ **Overnight fast:**

Ten hours before you are to have an OGTT or IVGTT test, you will need to stop eating/drinking. You can *and should* drink plain water during this time to prevent your body from becoming too dry (dehydrated).