

β Cell Function and Glucose Counter-regulation during the Progression of T1D

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Brief Description:

- The purpose of this study is to improve the lives of people with type 1 diabetes.
- We are studying people with T1D with varying amounts of remaining insulin secretion to see how much is needed to impact how glucose and insulin is handled in your body
- **Insulin**-is responsible for allowing your body to access the energy available from food, secreted from beta cells of the pancreas
- Type 1 diabetes occurs when the immune system destroys beta cells over time. While everyone with T1D must use insulin to control their blood sugar, recent research shows that small amounts of beta cells may still be making insulin even years after the diagnosis of T1D.
- We want to know whether these small amounts of remaining beta cells are helpful to people living with T1D.
- The study will last approximately 1 month and will include 4 study visits
- You will receive compensation in gift cards for each study visit, with the potential to earn \$500 in gift cards

Eligibility (enrollment pending)

You may qualify for participation in this study if:

- You are between the ages of 18 and 65 years old
- Have had a T1D diagnosis at least 2 years ago
- Recent HbA1c was < 9.0%
- You are willing to refrain from use of non-insulin agents to control hyperglycemia during the study

You likely DO NOT qualify for the study if:

- You have been diagnosed with impaired kidney function or impaired liver function
- You have been diagnosed with adrenal insufficiency
- You have active cardiovascular disease
- You have a history of seizure disorder not related to fever or hypoglycemia
- You take any of the following medications: systemic glucocorticoids, systemic progestin only contraception, atypical anti-psychotic agents, and beta-adrenergic blocking agents
- You have had an episode of severe hypoglycemia or diabetic ketoacidosis in the past 3 months
- You have been diagnosed with anemia

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Study Procedures

Visit 0 (Screening)

The first visit is a screening visit to be sure that you are eligible for the study.

The study team will:

- Ask you questions about your health, including any medical conditions you have and medications you take, and any other information that is needed to determine if you are eligible for the study.
- A physical exam may be performed if needed, including the determination of height, weight and blood pressure.
- An electrocardiogram (“ECG”/ EKG”), a test that checks the electrical activity of your heart, will be done.
- Approximately 3 tablespoons of blood will be drawn
- This visit will last about an hour
- You will be compensated with a \$50 gift card for this visit

Visit 1 (MMTT & CGM)

At this visit, you will:

- Undergo a 2-hour Mixed Meal Tolerance Test (MMTT)
- Have a continuous glucose monitor (CGM) placed.
- About 25 teaspoons of blood will be drawn during this study visit.
- This visit will last about 3 hours

Mixed Meal Tolerance Test (MMTT)

- You will need to come in for the test the morning after an overnight fast of at least 10 hours.
- Blood samples will be obtained throughout the test. To make the blood sampling easier, an intravenous needle and plastic tube (called an IV) will be placed in a vein in your arm. The IV will be kept in place during the test.
- You will be given a drink called BOOST[®]. The Boost drink is a “mixed meal” made of fats, proteins, and carbohydrates that looks (and tastes) like a milkshake.
- This drink will raise your blood sugar and cause your body to try to produce insulin. You will need to finish the drink within 5 minutes.
- This test will take about 2 hours and you will receive a \$100 gift card

Continuous Glucose Monitor (CGM)

- At the end of the meal test, you will have a continuous glucose monitor (CGM) placed on your belly and you will wear it for up to a week. The CGM will be inserted by a member of the study team who will instruct you on how to care for it at home.
- The CGM that you will be provided with is called the Dexcom G4[®] Platinum Continuous Glucose Monitoring System. This device is approved by the Food and Drug Administration (FDA).
- The CGM will be “blinded” which means the sugar levels it is reading will not be visible to you. However, we will review your sugar levels and patterns with you by the end of the study.
- During the time you are using the CGM, you will need to check your blood sugar at least 3 times per day with your home blood glucose meter.
- The placement of the CGM and patient instructions will take approximately 1 hour and you will be given a \$100 gift card

Visit 2

Arginine Stimulation Test (AST)

- This test is another way of measuring insulin secretion
- One IV will be placed in each of your arms. One side is for blood collection and the other for the infusion of glucose and arginine.
- Glucose will be given into the IV tube to raise your blood sugar level to around 230 mg/dl. After about 45 minutes from when the glucose is given, we will then give you arginine.

- **Arginine**-is an amino acid that also makes your body produce insulin. The arginine will be given through the IV over one minute and blood samples will then be drawn from the other arm IV over the following 5 minutes.
- Approximately 10 teaspoons of blood will be drawn
- The visit will last about 2 hours
- You will be given a \$100 gift card after test completion

At the end of the test, the study team will advise you regarding insulin and you will be offered breakfast.

Visit 3 (Hyperinsulinemic Euglycemic - Hypoglycemic clamp)

- During this visit, you will undergo a Hyperinsulinemic Euglycemic - Hypoglycemic clamp. The clamp test got its name because during the test, your glucose is “clamped”, or held, at a certain level so that we can see how your body responds to insulin.
- The first part of this test (Euglycemic part) measures how your body uses insulin when your blood sugar levels are normal.
- The second part of the test (Hypoglycemic part) measures how your body responds to hypoglycemia (low blood glucose).
- The clamp test will be done in the Clinical Research Center (CTRC) in the Hospital of the University of Pennsylvania.
- This visit will last about 7-8 hours and approximately 1 cup of blood will be drawn
- You will be given a \$150 gift card for this visit

During the Clamp Test

- For the “Euglycemic” part of the clamp test, you will receive a chemically modified glucose called a stable isotope through the IV. Two hours later, you will receive both insulin and glucose with the goal to keep your blood glucose levels at 90 mg/dl for 2 hours.
- For the “Hypoglycemic” part of the clamp test, we will gradually lower your blood glucose level to 50 mg/dl and keep it there for 2 hours.
- During the clamp test, your blood glucose level will be checked frequently and blood samples will be drawn regularly
- You will be given lunch after the test is over. The study team will help you with your insulin dosing, if needed.

What are the possible risks or discomforts?

Blood draw and IV Risks

The risks of having blood drawn and IV's placed include discomfort, bruising, infection, fainting, blood clots, or infiltration of the IV solution, which could cause skin burn or tissue damage. You may be offered numbing cream to help decrease any discomfort during a blood draw. However, these risks are very small and will be minimized by having experienced nurses and doctors continuously monitor the IV sites during the studies.

Continuous Glucose Monitor (CGM) Risk

The risks of wearing the CGM are minimal. Bruising, redness, discomfort, and some bleeding can occur. Mild skin irritation is common. Rarely an infection can occur at the site of CGM sensor needle placement. Any infection, or sign of infection, will be treated immediately. An allergic reaction to the tape used to hold the sensor in place is possible. If there is pain, redness, irritation, or rash at insertion site, the sensor will be removed and re-inserted in a different site.

Mixed Meal Tolerance Test (MMTT) Risk

There are no known risks to the MMTT, but you may not like the taste of the Boost drink, and you may also experience nausea.

Arginine Stimulation Test (AST) Risk

There may be a metallic taste in your mouth about 10-15 seconds after the Arginine is given. If this occurs, this metallic taste will last for less than 5 minutes. You may also feel burning and/or redness at the needle site where the Arginine is given. Rarely, an infection or swelling may occur.

Clamp Test Risks

The second part of the clamp study is designed to have your blood glucose levels drop to 50 mg/dl. You may feel lightheaded, dizzy, nauseous, sweaty, jittery, tired, or experience blurred vision from having your blood glucose changed. There is a small risk that your blood glucose becomes extremely low for a prolonged period. If this happens, it could cause a seizure. To minimize this risk, blood glucose will be monitored throughout the test. We will rapidly correct the low blood glucose by giving you glucose through your IV or by mouth to return blood glucose levels to normal.

Reproductive Risks

You cannot participate in this study if you are currently pregnant or become pregnant at any time during the study.

If you are sexually active, you must use medically accepted methods of birth control while you are on this study.

Privacy Risks

There is the unlikely chance that your information is viewed by someone outside the research team who is not authorized to see your health information. However, we make special efforts to make sure that this does not happen.

Loss of privacy from device downloads

Data downloaded from your insulin pump, BGM and CGM will be collected for the study as measures of diabetes self-management behaviors. Some people may be uncomfortable with the researchers having such detailed information about their daily diabetes habits.

Unknown Risks

There also may be side effects or risks that are not known at this time. If we become aware of any new risks, you will be told about them.

****By participating in this study you will automatically become a part of the T1D Exchange Clinic Network through the T1D Registry. Enrollment into the Registry will not occur until the β Cell Function study has ended. If you decide you do not want to be a part of the Registry, you may notify the study coordinator and you will be withdrawn from the Registry.**