

Procedures/Risks: endocrinology_template

Clamp Studies

Procedure: A procedure called a **glucose clamp** will be conducted during the study. During a glucose clamp, insulin (a hormone that helps the human body control sugar) and sugar (e.g., glucose) are given into one intravenous catheter (IV) and blood is drawn every 5 min through the other IV to determine how much sugar is in your blood. Two different rates of insulin will be given during the clamp. The first will be a low dose and the second a high dose. Each dose will be given for 150 min. The amount of sugar given will be adjusted to keep your sugar normal for the entire time. Every 30 minutes the blood pressure cuffs will be inflated to measure how much blood is going to your arm. During the study visit a maximum of 10 tablespoons of blood will be taken.

Procedure: Euglycemic Clamp and indirect calorimetry allows researchers to 1). examine whether insulin directly affects certain chemical in the body; 2). examine the relationships between these chemicals and the boy's use of carbohydrate, fat and protein, and; 3) examine the effects of insulin on the chemicals and gene function in skeletal muscle and fat tissue. During this procedure you will lie flat on your back in a bed. A nurse on the [insert name of research facility, e.g., The Ohio State University Clinical Research Center] will explain the procedure to you. Your nurse will insert two (2) intravenous (IV) lines (plastic tubes used to draw blood) into the veins (blood vessels that carry blood to your heart in the body) into your arms (one in each arm). One IV line will be to draw blood; the other to give medication. You will have a clear plastic dome placed over your head by your nurse while you lie flat in bed. This dome will be connected to a machine that will allow the researchers to measure the amount of oxygen you breathe in and out. When the test begins, one of your hands will be placed in a "warm box". The purpose of the warm box is to keep your blood temperature constant throughout the test. You will be asked to lie quietly for 20-30 minutes. After this "resting" period the test will begin.

The nurse will then give you an IV glucose solution that contains a substance that allows the amount of glucose in your blood called D3-3H glucose or tritiated glucose, to be measured. The amount of radiation in tritiated glucose is equal to that of a chest x-ray. This substance will allow the researchers to measure the rate at which glucose appears and disappears in your blood. This solution gets slowly broken down in your body and then leaves the body through the urine within 24 hours. Both insulin and glucose will be administered throughout the study. You will be given another medication in your IV line called Sandostatin. This medication will slow down or stop the natural production of insulin in your body. The nurse will monitor your blood frequently and make adjustments in the level of glucose that enters into your bloodstream through the IV line. The IV insulin will be delivered at a constant rate for 120 minutes. The blood glucose will be measured frequently to adjust the levels of the glucose being delivered into your body. Blood samples for glucose, hormones secreted by your pancreas (c-peptide, glucagon and insulin) and free fatty acid will be taken at 20 minute intervals for 240 minutes. Approximately 10 ml of blood per tube or $24 \times 10 = 240$ ml of blood will be kept for research tests. There will be 1 ml of blood discarded per blood draw (24 ml). The total amount of blood drawn that will be drawn will be about 264 ml which about the same as 18 tablespoons of blood.

Risks: Having intravenous catheters (small plastic tubes) placed in your arm(s) may cause pain, bruising, and infection.

The tests to measure blood flow and blood vessel function may cause discomfort, numbness, or tingling in the hand or arm. If you experience too much discomfort, then the study will be stopped.

Giving insulin and sugar water may cause your blood sugar to go to low or to high. High blood sugar will make you urinate more and thirsty. Symptoms of low blood sugar are sweating, shaking, anxiety, hunger, and confusion. If the sugar level goes too low coma and seizure, brain damage, and death are possible. Rarely does a person have an allergic reaction to the insulin. Should your blood glucose levels go too high or too low, medical treatment will be immediately available.

Frequently sampled intravenous glucose tolerance test (FSIVGTT)

Procedure: Frequently sampled intravenous glucose tolerance test (FSIVGTT) is a four-hour test that allows the researchers to see how your body responds to insulin, the hormone that helps blood sugar get into your body cells. For this test, a research nurse [at the Clinical Research Center (CRC)] will insert a catheter into a large vein in each of your arms. A catheter is a flexible plastic tube that will remain in your vein for the duration of the blood test to allow the nurse to take multiple blood samples from the same site without having to stick you with a needle each time. One arm vein will be used to have solutions of sugar and insulin go into your body through the catheter. The other arm will be used to collect frequent blood samples. After first blood samples are taken (at 0 minutes), the nurse will give you glucose [at a constant rate over 2 minutes] in an amount in proportion to your body weight. Twenty minutes after the start of the test, the nurse will inject a dose of human insulin also determined by your body weight. The nurse will take frequent samples of blood over the four-hour period. You will be resting during this entire four-hour procedure. The total volume of blood to be drawn for each FSIVGTT is 245 milliliters (a little more than one cup).

Procedure: The frequently sampled intravenous glucose tolerance test or FSIVGT, is a test that measures how well your body responds to a high dose of intravenous (IV) glucose and insulin. You will not eat or drink for 10-12 hours the night before the test [but a snack will provided to you after completion of the tests at this visit]. You will report to the [insert name of research facility, e.g., The Ohio State University Clinical Research Center]. Your nurse will explain the procedure to you. You will be instructed to lie flat in bed on your back. The nurse will insert two (2) intravenous (IV) lines (plastic tubes for drawing blood) into your veins (blood vessels that carry blood to your heart in the body) one in each arm. The nurse will draw four (4) tubes of blood over 20 minutes. After this, the nurse will give you an IV injection of glucose. After 20 minutes, the nurse will inject insulin into the IV line. Blood samples will be collected frequently over a 180 minute period - (total of 20 tubes). There will be about 10 milliliters of blood per tube or $20 \times 10 = 200$ milliliters of blood. In addition 1 ml of blood will be discarded

per blood draw (20 ml). Total blood volume = 220ml of blood. This is equal to approximately 15 tablespoons of blood.

Procedure: You will receive a Frequently Sampled Intravenous Glucose Tolerance Test (FSIVGT). This test will assess your body's ability to respond to intravenous (IV) glucose and insulin. You will have two intravenous catheters (IVs) placed in your arm. You will have a sugar solution and insulin injected into your veins through one IV. These solutions will change the glucose (blood sugar) level in your blood. Blood samples for glucose and insulin [and C-peptide (hormones produced by your body)] will be drawn from the other IV to measure how your body uses glucose and insulin. Blood will be drawn a total of 19 times during the FSIVGT. During this test a total of approximately 6.5 ounces or about 12 2/3 tablespoons of blood taken

Risks: You may experience some degree of discomfort, swelling, bruising, lightheadedness, and, on rare occasions, infections with [finger-stick blood collections, fasting blood draws, oral glucose tolerance testing, and] frequently sampled intravenous glucose tolerance testing. To minimize risks, you will be seated or lying down for all blood collections and the research nurses will use sterile techniques and supplies for all blood collection procedures.

You may experience nausea, lightheadedness, or hypoglycemia as a result of fasting overnight for a minimum of 10 hours before the selected study visits [identify visits]. The researchers will encourage you to monitor your blood sugar at home in the morning, prior to coming for study visits. If you experience any of the symptoms described above or if your blood sugar measurement after fasting is less than 70 milligrams per deciliter, you should consume 15 grams of carbohydrate and call the researchers to reschedule your study visit. At the start of each visit, the research nurses will also check your blood sugar using the finger-stick method. If you repeatedly experience hypoglycemia (low blood sugar), the study doctor may need to adjust your medications or you may need to discontinue participation in the study.

Hyperglycemia (high blood sugar) or hypoglycemia (low blood sugar) may result after the [oral glucose tolerance test or the] frequently sampled intravenous glucose tolerance test. At the end of these blood tests, the research nurses will check your blood sugar using the finger-stick method. If you are hypoglycemic, you will be given some food containing glucose and monitored until your blood sugar has reached a normal range at which time you can then leave. A meal will be provided after study procedures are completed. If you are hyperglycemic at the end of the study visits, the study doctor may recommend a dose of insulin to bring your blood sugar down. For your safety, you will be monitored by the research team while at the site until it is felt that you are able to be released to go.

Risks: The discomforts associated with the FSIVGT include blood drawing and intravenous catheter (IV) placement. There is potential for pain, bleeding, fainting, bruising, infection and/or hematoma (blood clot under the skin) at the IV site. This is temporary and can be treated with warm compresses and/or antibiotic medication, if necessary. These risks will be minimized by

using well trained and experienced medical personnel. There is a risk involved with the injection of insulin through the vein. This can lead to the blood sugar dropping too low. This will be treated if and immediately when it occurs. The symptoms associated with blood sugar that is too low are dizziness, confusion, sweatiness, irritability, and the sensation of heart racing. These symptoms go away with the appropriate treatment and will not cause any permanent problems, because the low blood sugar will be treated immediately.

Glucose monitoring

Procedure: You will be given a glucose meter and testing supplies. You will be asked to measure your blood sugar levels three times per day: before breakfast, before bed, and 2 hours after lunch or dinner. You are to record the levels in a diary. You will also be asked to test your blood sugar anytime you feel it is low. If you are currently taking insulin, your insulin doses will be adjusted to keep your blood sugars in the normal range.

Hypoglycemia

Hypoglycemia is caused by a drop in the body's blood sugar level. Some of the symptoms of hypoglycemia are being dizzy, tired, restless, hungry, and unusually irritable. Other symptoms may include difficulty concentrating, sweating, tremor (shaking), nausea and sensation of rapid or irregular heartbeats. If you have any of these signs, then you need to check your blood sugar and then drink some fruit juice to raise the blood sugar level. If the symptoms continue or you have any questions, then contact your study doctor. If you take insulin, your study doctor will give you instructions on how to prevent hypoglycemia.

Intravenous (IV) insulin injection

Procedure: A needle with a plastic tube attached will be inserted into a vein in your arm. This is known as an intravenous line or "IV". Through this IV [study] insulin will be administered over a period of time. Insulin is a hormone produced by your body. IV insulin may cause your blood glucose [sugar] levels to drop.

Risk: Insulin is a hormone produced by the pancreas in your body. IV insulin may cause your blood glucose levels to drop. You may feel lightheaded or nervous. There may be pain, burning, inflammation (swelling/redness) at the IV site. To minimize these side effects, the medication will be administered slowly. Your blood glucose (sugar) will be checked frequently. To minimize these side effects, you will be give oral (by mouth) or IV glucose to correct the low blood glucose.

The Intravenous (IV) insulin injection that is to be injected during the experimental test can cause low blood sugar reactions and symptoms. These symptoms may include nervousness, sweating, confusion and in severe cases, coma. If the symptoms are mild and you are awake and alert, you will be asked by the nurse to drink a liquid that has sugar in it. If the symptoms are severe you will receive glucose (sugar) in your vein to raise you blood sugar. This risk is lessened by having trained nurses test your blood sugar level frequently during the test.

There is minimal radiation exposure with the administration of tritiated glucose during the experimental testing procedure. Tritiated glucose is broken down and excreted in the urine within 24 hours with no harm to body tissues. The National Radiation Commission reports no evidences of triated glucose-related tissue injury.

There is a risk of low blood sugars. You will be treated with glucose by mouth or through the IV if this occurs. You should tell your nurse if you experience any unusual symptoms that might signal low blood sugar, such as nervousness, shakiness, sweating, or racing heart. In general, the duration of any low sugars is expected to be short, because you will be undergoing regular monitoring. Therefore, it is very unlikely that you would experience any permanent damage if it occurs. However, very rarely, it is possible that extremely low blood sugars could trigger a heart attack or stroke. The risk of low blood sugar is present with *any* form of insulin therapy, whether or not you agree to participate in the current study.

There is also a risk of high blood sugars, because your insulin needs might change from day to day [, and also because the [study medication] could wear off early in some people]. You will be given supplemental short-acting insulin to treat the high level of sugars in your blood. In addition, your dose of [study medication] will be adjusted to bring the sugars down. It is possible that you could experience very high sugars and require a second insulin infusion for a longer duration. If this happens, you may be withdrawn from the study.

Mixed meal test (24 hour meals profile)

Procedure: This test will allow researchers to measure what foods do to the body and how foods are utilized by the body. For this procedure you will be admitted to the [insert name of the clinical research facility, e.g., The Ohio State University Clinical Research Center] on the evening prior to the test [or early in the morning on the day of the test (6:00am)]. You will be required to *not* eat anything for 10-12 hours *prior* to the test. At 7:00 am on the day of the test, the nurse will insert two (2) intravenous (IV) lines (plastic tubes used to draw blood) into the veins (blood vessels that carry blood to your heart in the body) in your arms (one in each arm). Blood samples will be drawn [at – insert time point(s)]. You will be asked to consume a standard [Healthy Choice] breakfast at 8:00am, lunch meal at 12pm, and dinner meal at 6pm. Blood samples will be drawn every XX minutes from 7:30 am until 8am the next day (24 hour profile) to measure the concentrations of various chemicals in your blood.

Risk: The mixed meal is a standard prepared meal. There are no known risks to eating this meal; however, it is possible that you may not like the type of foods and/or the taste of those foods included in the meal.

Oral Glucose Tolerance Testing

Procedure: During this study, you will undergo an oral glucose tolerance test. This is a three-hour test that involves several blood samples. For this test, you will have a catheter (thin plastic tube) inserted into a large vein in your arm. A catheter is a thin, flexible, plastic tube that will be inserted with a needle and can remain in your vein during the study visit. The catheter will allow the study nurse to draw several blood samples from your vein without reinserting a needle each

time. You will be asked to drink a sweet, orange-flavored beverage (“Glucola”) in 10 minutes. The time at which you begin drinking the beverage will count as “0 minutes.” The nurse will take a total of [11] small samples of blood from your vein during the three-hour test (three times before I drink the beverage and eight times after I drink the beverage). The first blood sample will be a maximum volume of 30 milliliters (2 tablespoons). Each of the remaining samples will be a maximum of 10 milliliters (2 teaspoons) of blood per sample. The total amount of blood required for this test is about ½ cup. The results of the oral glucose tolerance test will allow the researchers to observe how your body reacts to sugar.

To see how well your body uses sugar, you will have an oral (by mouth) glucose tolerance test. For the glucose tolerance test you will drink about 10 ounces of glucose (sugar drink), and will have blood drawn 30 minutes, 1 hour, 2 hours, and 4 hours after I drink the glucose. The glucose is like a sweetened flavored drink.

Before you have the three-hour OGTT, the nurse will give you a handout that describes how to prepare for the test. On the morning of the test, the nurse will draw one tube of blood from your arm soon after you arrive. During this blood draw, she will insert a small catheter (thin plastic tube) into your vein that will be used to collect the remainder of the blood samples so that you will only have to be stuck with a needle one time during the test. She will then give you an 8-ounce bottle of liquid to drink that has a large amount of sugar in it. Once every hour for the next three hours the nurse will collect a blood sample from the catheter.

Procedure: On the night before your test, you should not eat or drink anything for 10-12 hours. A history and physical examination will be performed by one of the physicians involved in the study before this test is conducted.

After the consent has been signed a nurse will instruct you to lie on your back comfortably in a bed. An intravenous (IV) line (plastic tube used to draw blood) will be inserted into your arm. The nurse will draw blood samples for various chemicals in the body [glucose (sugar in the blood), insulin, c-peptide (hormones produce by the pancreas), cholesterol, fatty acids (fat in the blood) and adiponectin levels]. [You also will have blood samples obtained to measure substances derived from fat cells that have been associated with type 2 diabetes, high blood pressure and heart disease]. The nurse will then give you a sugar substance to drink over a 2 minute period. Blood samples will be drawn every 30 minutes for 180 minutes.

Risks: You may experience hyperglycemia (high blood sugar) as a result of the oral glucose tolerance test.

Study staff will check your blood sugar levels from a drop of blood at the end of the oral glucose tolerance test. If your blood sugar is high, then the Study Doctor will be contacted for further advice. The Study Doctor may recommend that you receive a dose of insulin to bring your blood sugar down to normal levels.

Risks: You may find it difficult to drink the extremely sweet glucose [sugary] liquid. Some people feel sick after drinking the glucose liquid and may vomit. Vomiting may prevent you from completing the test on that day.

The blood sample is taken from a vein in your arm. An elastic band is wrapped around your upper arm. It may feel tight. You may feel nothing at all from the needle, or you may feel a quick sting or pinch. You may feel faint from having several blood samples taken in one day. However, the amount of blood taken should not cause significant blood loss or anemia.

It is possible that your blood glucose levels may drop very low toward the end of the test. Symptoms of low blood glucose include weakness, hunger, sweating, and feeling nervous or restless. If you develop these symptoms during the test, you may have your sugar level checked quickly with a glucose meter. If your level is very low, the test will be stopped.

Reactive hyperemic response

Procedure: **Reactive hyperemic response** will be studied by placing 2 blood pressure cuffs on your non-dominant arm (left arm if the subject is right handed). One cuff will be placed on the arm at the wrist and one will be placed on the upper arm. During measurement the wrist cuff is inflated to block blood flow to the hand and the upper arm cuff is inflated for 10 out of every 15 seconds to block blood flow leaving the arm. Forearm blood flow is obtained by measuring arm expansion with a specialized gauge. Arterial blood pressure will be continuously monitored in the dominant arm (right arm if the subject is right handed).

For each subject two minutes of baseline flows will be recorded and then the upper arm cuff will be inflated to 200 mmHg pressure for five minutes to occlude flow to the arm. It will then be released and forearm blood flow will again be measured for the next 2 minutes.

Procedure: For this test two blood pressure cuffs will be put on your arm. One will be put at the wrist; the other will be on the upper arm. An elastic wire will be put around your forearm. This equipment is used to measure the blood flow to your arm. When the blood flow is being measured the cuff on the wrist will be inflated to a high pressure to temporarily stop blood flowing to your hand and the cuff on the upper arm will be inflated at low pressure off and on every 15 seconds. This will be done for 2 minutes. The upper arm cuff will then be inflated to a high pressure to cut off blood flow to the arm for 5 minutes. It will then be released and the blood flow to the arm will be measured again for 2 minutes. A machine which measures arterial blood pressures called an arterial tonometer will be put on your other wrist during the entire time. This part of the protocol will take approximately 10 minutes to set up, 9 minutes to perform and 5 minutes to take down. The blood flow to your hand will be stopped for a total of 9 minutes and to your child's upper arm for 5 min.

Risks: The stopping of the blood supply to your hand for a total of 9 min and to the forearm for 5 min may make your hand feel numb or tingle. The feeling will go away when the pressure is released. If this becomes too uncomfortable you can ask the investigators to stop.

Skin blister Test

Procedure: Eight small blisters (8 millimeters in diameter-each about the size of a pencil eraser) will be gently formed on your nondominant forearm. This process will take about 1-1 ½ hours. It is done by using a blister template (a pattern with eight holes that are about the size of a pencil eraser) and a suction machine. After the blisters are formed, a small plastic dome will be secured over the blisters for protection. The fluid will be removed from 4 of the blisters after 12 hours and from the other 4 after 24 hours. The blister tops will be gently removed with sterile scissors. The fluid will be evaluated to see if certain substances that affect wound healing are different between the groups. A light bandage will be placed over the blisters before you are discharged. You will be given instructions about how to care for the blister wounds.

Risks: You will feel a pulling or sucking like sensation as the blisters are being formed. The heat involved in the blister formation is approximately 104 degrees F. Neither the heat nor suction should cause you discomfort. There is minimal discomfort from the two needle sticks. The blistering procedure involves only the top layer of tissue, so there should be no scarring. There is rapid healing of this layer with a very low risk of infection. Specific wound care instructions will be provided to minimize the risk of infection.

Thymectomy

Procedure: The surgical procedure is performed under general anesthesia and involves making a vertical (“up and down”) incision in the front of the chest, dividing the breast plate. The thymus gland is located underneath the breast plate and is removed during the surgery. Fatty tissue around the gland is also removed to make sure that smaller collections of thymus tissue are removed. The operation may be followed by pain and discomfort for several days which can be well controlled with pain-relieving medications. A noticeable scar does result from the procedure.

Risks: Thymectomy may be associated with complications (problems), but it is not possible to predict whether they will happen or not. Information about known problems is based upon past experiences and studies of individuals who have had thymectomy.

- 10 and up to 50 people out of 1,000 have had these problems: bleeding requiring one or more blood transfusions, dependence on a mechanical ventilator for several to many days following the surgery, injury to the phrenic or recurrent laryngeal nerves resulting in weakness of a breathing muscle or hoarseness.

- Fewer than 10 people in 1,000 had these problems: a serious infection requiring re-operation, prolonged lymph drainage from a lymphatic duct in the chest cavity requiring a drainage tube, or death from surgical complications.
- As with any surgical procedure that involves an incision (cut deep below the skin), it is typical for patients to have pain and discomfort in the region of the chest incision. This should be mild by the time of hospital discharge and minimal for several weeks after the surgery. You will be given standard medications to minimize the postoperative discomfort.