L'Hôpital de Montréal pour enfants
The Montreal Children's Hospital
Centre universitaire de santé McGill
McGill University Health Centre

PEDIATRIC RESEARCH INFORMATION AND CONSENT FORM

Title : Peanut and Tree Nut Desensitization and Induction of Tolerance in Children

Name of Participant :

Persons responsible : Dr Moshe Ben-Shoshan_

Dr Bruce Mazer

Funding Source: __Fast Foundation, Montreal Children's Hospital Foundation

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS STUDY?

The Allergy department participates in research studies to try to improve treatments for children with peanut or tree nut allergy. Today, we are inviting you to take part in a research study. Please read this information to help you decide if you want to participate in this research project. It is important that you understand this information. We encourage you to ask questions. Please take all the time you need to make your decision.

We encourage parents to include their child in the discussion and decision making to the extent that the child is able to understand.

In this research information and consent form, "you" means you or your child.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to assess a treatment protocol that may help children with peanut or tree nut allergy tolerate peanut or tree nuts. This process is called Oral Immunotherapy and involves 2 treatment periods: 1) gradual supervised exposure to peanut or tree nut in our research unit; 2) Supervised exposure to peanut or tree nut at home. We also want to see if lower doses of peanut or tree nut are as effective in attaining tolerance to peanut or tree nut as higher ones.

BACKGROUND

You have peanut or tree nut allergy. Typically with patients with food allergies, treatment consists of avoiding the allergenic food and managing reactions when they occur, but not of removing the actual allergy. Recent studies have shown that people with food allergies can be made 'tolerant' (meaning they won't react) to foods to which they had previously reacted by very slowly introducing the allergenic food. We want to see if by using our protocol, we can make patients who are allergic to peanut or tree nut tolerant to peanut or tree nut. FOR THIS RESEARCH PROJECT, YOU WILL ONLY UNDERGO DESENSITIZATION TO ONE ALLERGEN: IF YOU ARE ALLERGIC TO PEANUT, YOU WILL UNDERGO DESENSITIZATION TO PEANUT. IF YOU ARE ALLERGIC TO A TYPE OF NUT, YOU WILL ONLY BE DESENSITIZED TO THAT TYPE OF NUT. IF YOU'RE ALLERGIC TO SEVERAL TYPES OF NUT, YOU WILL CHOOSE TO WHICH TYPE OF NUT YOU WANT TO BE DESENSITIZED.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 75 patients will take part in this study. Approximately 50 will come from this hospital, with the other patients coming from centers across Canada.

WHAT WILL HAPPEN ON THIS RESEARCH STUDY?

The desensitization progress consists of three stages: a blinded, oral food challenge, an escalation/home dosing phase and a maintenance phase. After the first stage, the blinded oral food challenge, you will be randomly assigned (like flipping a coin) to one of three groups: group A, B or C. Patients randomized to the treatment group A will begin oral desensitization as described below. Over the course of approximately 5-6 months, patients in this group will take larger and larger doses of peanut or tree nut protein until they can tolerate a 300 mg dose of peanut or tree nut protein. The protein will come from crushed peanut or tree nut. Patients randomized to group B will also begin oral desensitization. However, children in this group will only increase their doses for approximately 6 weeks, up to a 30 mg dose of peanut/tree nut protein. They will then remain on this dose for another 16 weeks. All participants in Groups A and B will be blinded to which group they are assigned. That means you will not know if you are in Group A or Group B. Patients in group C will not undergo oral-immunotherapy, but will be followed for one year following their oral food challenge. Patients undergoing oral immunotherapy will be asked to complete a daily symptom diary documenting your symptoms during the study period. These will take no more than 5 minutes per day to complete. In addition, a sample of 5-10 ml of blood (less than one tablespoon) will be taken from a vein in your arm and 5 ml of saliva initially and during the follow-up period (every 3 months for 1 year). We are collecting the blood and saliva samples in order to track the changes that are taking place in your immune system during the desensitization process. We hope that the results from these analyses will in the future enable us to determine who might tolerate oral desensitization better. Finally, you will have to do skin prick testing to measure your allergy to peanut or tree nut. If desensitization proves effective, children in the follow-up only group will be invited to participate in oral immunotherapy after the follow-up year. We will also review your medical records at the Montreal Children's Hospital.

You will be contacted every 1-3 months by our research team (either by email or phone according to your preference) during the following year and be asked about accidental exposure and potential allergic reactions.

ORAL IMMUNOTHERAPY (OIT)

Oral Immunotherapy for peanut or tree nut is a way to allow people with peanut or tree nut allergy to avoid anaphylactic reactions when accidentally exposed to a small amount of the foods to which they are allergic. The goal of this study is NOT to have you incorporate peanuts or tree nuts into your regular diet. . There are four stages to Oral Immunotherapy (OIT).

Blinded Oral Peanut or Tree Nut Challenge

The first stage of OIT is a blinded oral peanut or tree nut challenge. This is done to be absolutely sure that you are allergic to peanut or tree nut. We need to do this to make sure you are eligible for this study. The challenge will take place over two days and is placebo controlled (a placebo is a substance with no active ingredients that you should not have an allergic reaction to). This means that one day you will receive increasing doses of placebo, and one day you will receive increasing doses of peanut or tree nut. You will not know whether you are receiving peanut or tree nut, or placebo on either day, as we will be mixing the doses in a product like pudding or apple sauce to disguise the taste. Both days' challenges will take place in Center for Innovative Medicine (CIM) in the hospital.

There are pairs of nuts whose allergens have similar protein structures. This means that people who are allergic to one of these nuts are often allergic to the other nut in the pair as well. Walnuts and pecans are an example of one of these pairs, as are pistachio and cashew. We would like to see if becoming desensitized to one of these nuts will mean that you become desensitized to the other nut in the pair as well. If you agree to this part of the study, at the challenge phase, you will be challenged to one of the nuts in the pair then four weeks later, we will challenge you to the second nut in the pair. . You would not start your desensitization until after the challenge to the second type of nut. You will undergo desensitization to only one of these nuts. At the end of the desensitization process, when it comes time for the post-escalation challenges, you will undergo challenges to both nuts, again with the challenges separated by four weeks. If you agree to this extra part of the study, it means that you will have two extra challenges. We will then be able to see if desensitization to the first nut has changed your sensitivity to the second nut.

The way the challenges work is as follows:

1. You will come to the CIM in the morning. You will have an intravenous line put in your arm. This is so that if you have an allergic reaction, medication to treat the reaction can be given as quickly as possible.
2. Once you have the intravenous put in, you will be given a small dose (0.1 ml) of either peanut or tree nut protein or placebo (a product to which you are not allergic). You will not be told which one you are getting.
3. Every 30 minutes, you will be given a larger amount of peanut or tree nut protein or placebo, up to 100 mg.
4. If the study doctor feels that you are having an allergic reaction, the challenge will stop, you will be given medication to treat the allergic reaction and will not take any more of the product.
5. To ensure that you are safe and don't have a late reaction, you will stay at the CIM under the observation of the study staff for at least two hours after the end of the challenge. If you react to peanut or tree nut, you will be considered to have had a positive challenge, and thus be eligible for the study.

After the Blinded Challenge, you will be randomly (like flipping a coin) assigned to either Group A, B or C, as mentioned above.

Rush Desensitization

This phase is where you start being exposed to peanut or tree nut, with the eventual goal of making you tolerant to peanut or tree nut (meaning that you will not have an allergic reaction to it if you eat some). This phase takes place over two consecutive days. As with the challenges, this will take place in the CIM. On the first day, you will start with a very small dose of peanut or tree nut protein (0.5 mg). Every 20 minutes you will be given a slightly bigger dose, until you reach 5 mg. After that last dose you will stay at the hospital for another hour, to make sure that you don't develop an allergic reaction. On the second day, you will receive a dose of 3 mg of peanut/tree nut protein. If you do not react to the peanut or tree nut protein during the Rush desensitization, we will supply you with peanut or tree nut protein and you will begin taking 3 mg of peanut or tree nut protein each day at home. Participants in both groups A and B will go through these phases in exactly the same way. Participants assigned to Group C will not do this part of the study.

Escalation/Home Dosing Phase

During this phase, you will start eating crushedpeanut or tree nut at home. As mentioned above, participants in Group A will start by taking 3 mg of peanut or tree nut protein at home every day. This will continue for two weeks. After two weeks, you will come to the CIM and, under the supervision of the study staff, will Increase your dose of peanut or tree nut protein. For the next two weeks, you will take this new, higher daily dose at home. At the end of two weeks, you will come back to the CIM and again under the supervision of the study staff, eat the next higher dose of peanut or tree nut protein. This dose will be consumed at home for the next two weeks. This process of coming to CIM and eating a slightly higher dose of peanut or tree nut and then eating this new dose at home will continue until you reach 300 mg This stage should take approximately 22 -30 weeks, depending on how well you tolerate your doses of peanut or tree nut protein.
If you are in Group B, you will do the same process as participants in Group A: you will start at 3 mg of peanut or tree nut protein, and you will come to the CIM every two weeks to increase your dose. You will take this dose at home for two weeks, then come back to the hospital to increase your dose again. Unlike participants in Group A however, this process of dose increases will only go to a maximum of 30 mg. This should take approximately 6 weeks. You will then stay on this dose for another 16 weeks, making for a total of approximately 22 weeks in the escalation phase.

Maintenance Phase

This phase will last twelve months.

Depending on which group you were randomized to, for the first three months of this phase you will eat either 30 mg or 300 mg of peanut or tree nut protein a day. After three months, you will come to CIM for another blinded oral peanut or tree nut protein challenge to see how well you are tolerating the peanut or tree nut protein. This will be similar to the one you did at the beginning of the study. After the challenge at 3 months post oral immunotherapy, you will continue taking the same dose of peanut/tree nut protein you have been taking, but you will only have to take the dose at least twice a week.

During the remaining nine months of the follow-up period, you will come to CIM on three more occasions, at 6, 9 and 12 months post Oral Immunotherapy. During these visits you will have skin, blood and saliva tests will be done. We are doing this to see how the changes in your ability to eat peanut or tree nut vary with markers in your blood and saliva as well with

allergy skin prick tests. At the last, 12 month visit, you will do one more blinded, oral food challenge. We are doing this to ensure that desensitization persists over time and even at less frequent dosing intervals

For participants in Group B, if you react to the peanut or tree nut protein during this challenge, this means that you were not able to be desensitized with 30 mg dose. You will re-enter the Escalation Phase and proceed like participants in Group A all the way up to 300 mg dose. You will then enter the Maintenance Phase just like patients in Group A.

Quality of Life questionnaires

We are interested to see what effect the peanut or tree nut desensitization has on how you view your peanut or tree nut allergy. To discover this, at four times during the study, we will ask you to fill out a quality of life questionnaire. This questionnaire has been specifically created to assess the effect food allergies have on a family's quality of life. The questionnaires will take about ten minutes to fill out, and will be given while you are here at the hospital for a scheduled study visit

FOR HOW LONG WILL YOU PARTICIPATE IN THIS STUDY?

Participation in the study will last about 18 months

WHAT ARE THE RISKS?

If you are assigned to the oral immunotherapy group, you might have allergic reactions during this treatment. These reactions can include nausea, abdominal pain, vomiting, or inflammatory disease of the esophagus (known as eosinophilic esophagitis. You may also experience skin symptoms such as hives or itchiness. Rarely, more severe reactions such as breathing problems may occur. These reactions can take place during any phase of the study. Your reactions will be monitored and treated promptly during the desensitization process in our allergy unit by our team and if deemed necessary by our medical team the therapy will be stopped. You will also receive detailed instructions for treating reactions should they occur during the home phase of therapy. All subjects on treatment will be given an adrenalin auto-injector (Epipen) as a precaution.

The risks of having blood drawn include pain where the needle is put in, minor bleeding, bruising, and fainting. A topical anesthetic (freezing) cream can be used to decrease the pain. All of these rarely occur and do not cause any long lasting problems.

SHOULD YOU SUFFER ANY HARM Should you suffer harm of any kind following administration of the study drug, or following any other procedure related to the research study, you will receive the appropriate care and services required by your state of health.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Your participation in this research may provide potential benefit if you are assigned to the oral immunotherapy treatment group and if the experimental treatment is successful. If you are not assigned to receive desensitization there will be no direct benefit. However, the information collected from this study may help us better understand and design future therapies. In addition, if you are randomized to group C and are interested in receiving oral immunotherapy, we will offer this treatment at the end of the first year of study enrolment.

WHAT OTHER OPTIONS ARE THERE?

Instead of participating in this research project, you could choose the standard treatment, of avoiding peanut or tree nut and treating the reactions if you are exposed to peanut or tree nut. Please discuss the different options you have with your doctor.

IS ANY COMPENSATION BEING OFFERED?

You will be reimbursed for the costs of parking related to your participation in this study. Other than that, you will not receive any financial compensation for participating in this research study

HOW IS PRIVACY ENSURED?

During your participation in this study, the study doctor and their team will collect and record information about you in a study file. They will only collect information required to meet the scientific goals of the study. The study file may include information from your medical chart concerning your past and present state of health, your lifestyle, as well as the results of the tests, exams, and procedures that you will undergo during this research project.

All the information collected during the research project will remain confidential to the extent provided by law. You will only be identified by a code number. The key to the code linking your name to your study file will be kept by the study doctor.

To ensure your safety, a copy of this information and consent form will be placed in your medical chart. As a result, any person or company whom you give access to your medical chart will have access to this information.

The study data will be stored for 25 years by the study doctor

The data may be published or shared during scientific meetings, however it will not be possible to identify you.

For monitoring, control, safety, and security, your study file as well as your medical charts may be examined by a person mandated by Canadian or international regulatory authorities, such as Health Canada, as well as by representatives of the study sponsor, the institution, or the Research Ethics Board. All these individuals and organizations adhere to policies on confidentiality.

You have the right to consult your study file in order to verify the information gathered, and to have it corrected if necessary

However, in order to protect the scientific integrity of the research project, accessing certain information before the project is ended may require that you be withdrawn from the study.

IS YOUR PARTICIPATION VOLUNTARY?

Your participation in this research project is voluntary. Therefore, you may refuse to participate. You may also withdraw from the project at any time, without giving any reason, by informing the study doctor or a member of the research team.

Your decision not to participate in the study, or to withdraw from it, will have no impact on the quality of care and services to which you are otherwise entitled, or on your relationship with the study doctor or clinical team.

The study doctor, or the Research Ethics Board, may put an end to your participation without your consent. This may happen if new findings or information indicate that participation is no longer in your interest, if you do not follow study instructions, or if there are administrative reasons to terminate the project.

However, before you withdraw from the study we suggest, that you return to the clinic for a final evaluation, for safety reasons.

Any new findings that could influence your decision to stay in the research project will be shared with you as soon as possible.

If you withdraw or are withdrawn from the study, the information collected during the study will nonetheless be stored, analyzed or used to protect the scientific integrity of the research project.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about this research project or if you suffer any problems you believe are related to your participation in this research, you can call the researcher responsible for the project in your hospital:

Montreal Children's Hospital: Dr. Moshe Ben-Shoshan at (514) 412-4470 (principal Investigator)

In case of emergency, please go directly to the closest emergency room.

If you would like information about your rights related to your participation in the research, you may contact the hospital Ombudsman (Patient Representative):

- Montreal Children's Hospital : 514-412-4400, poste 22223

RESEARCH ETHICS COMMITTEE

The Research Ethics Board of the McGill University Health Center approved this study and is responsible for monitoring it at all participating institutions in the health and social service network in Quebec.

Title of this research project: Peanut or Tree Nut Desensitization and Induction of Tolerance in Children

I have been explained what will happen on this study. I read the information and consent form of 8 pages including the annexes and was given a copy to keep. I was able to ask my questions and they were answered to my satisfaction. After thinking about it, I agree to, or I agree that my child will, participate in this research project.

I authorize the research team to consult my medical records or the medical records of my child to collect the information relevant to this project.

By agreeing to participate in this research project, you are not waiving any of your legal rights nor discharging the study doctor, the sponsor or the institution, of their civil and professional responsibilities.

☐ I consent to participate in the challenge with the second type of nut

Name of participant (Print)	Assent of minor, capable of understanding the nature of the research (signature) or Verbal assent of minor obtained by:	Date
	_____	

Name of parent(s) or legal guardian (Print)	Signature	Date

Local Study #_2017-3204_____
Date of this version: __March 15, 2018_____

Name of participant (18 years +) (Print) | Signature | Date

I have explained to the participant and/or his parent/legal guardian all the relevant aspects of this study. I answered any questions they asked. I explained that participation in a research project is free and voluntary and that they are free to stop participating at any time they choose.

Name of Person obtaining consent (Print) | (signature) | Date

Addendum to consent form

Participant who has now become an adult (18)

Title of research project : _____

Today, I reviewed the information and consent form that my parents signed on my behalf when I enrolled in this research project and a copy of that signed consent was given to me.

I agree to continue my participation in this research project.

I understand that my participation is free and voluntary and that I can stop participating in this research project at any time I choose.

I authorize the research team to consult my medical records to collect the information relevant to this project.

If I withdraw, any remaining samples or data that has not already been analyzed will be destroyed.

_____ _____ _____

Name of participant | Signature | Date

_____ _____ _____

Name of person obtaining consent	Signature	Date