CONSENT FOR A CHILD TO BE A SUBJECT IN MEDICAL RESEARCH AND AUTHORIZATION TO PERMIT THE USE AND SHARING OF IDENTIFIABLE MEDICAL INFORMATION FOR RESEARCH PURPOSES

TITLE Efficacy of Tympanostomy Tubes for Children with Recurrent Acute Otitis Media
Randomization Phase

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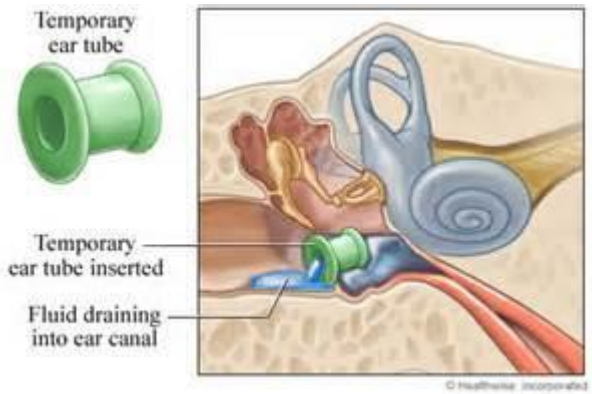
What is this study about and why is it being done?

We are asking you and your child to take part in our research study because your child has had several ear infections. Tympanostomy tube placement (or ear tubes) is a common surgical procedure performed for children who have multiple ear infections. We know that 7 out of every 10 children experiences at least one ear infection during the first year of life. Two out of every 10 children have multiple ear infections. These ear infections can be treated with antibiotics, but in some cases, placement of ear tubes is considered. Ear tubes are thought to prevent future ear infections by providing drainage between the middle ear and the outside. This procedure may not be the best answer for every child and some children improve without having the tubes placed in the ears. We are doing this study to determine which children are most likely to benefit from this procedure.

You have already participated in Part 1 of this study, the screening phase. Our study team has decided that your child has had either 3 ear infections in 6 months or 4 in 12 months. The study team saw your child for at least one of these infections. You and your child are now being asked to participate in Part 2 of this study, the randomization phase.

It is not clear what the best management is for children with multiple ear infections. There are two options, ear tube placement or continued treatment without ear tubes. Ear tube placement is accepted by many physicians in the US, but in other countries they do not agree that ear tube surgery is the answer. It is thought that ear tubes work by providing drainage between the middle ear and the outside. This allows any bacteria that would be behind the ear drum, to drain to the outside. By having the tubes in place, some ear infections may be able to be treated with antibiotic ear drops instead of taking antibiotics by mouth. However, the possible risks of surgery and complications that can occur after surgery should be considered when making this decision. This surgery may help some groups of children more than others.



What are my child and I being asked to do?

About 160 children in the Pittsburgh area, between the ages of 6 and 35 months will be randomized in the Part 2 study. If you enroll your child in Part 2, your child will be randomized to either have ear tubes (tympanostomy tubes) placed or to be closely observed without the placement of ear tubes. We do not know which the better choice is for your child. You and I can't pick which group your child will be in. A computer decides for us. There is a 50/50 chance that your child will be in either group. Your child will either be assigned to the group that has the surgery or the group that does not have the surgery. If your child is assigned to the group that gets ear tubes, the surgery will be scheduled within two weeks.

Your child will be closely followed for two years after the surgery. We will plan to schedule a visit about every 8 weeks. Study visits will be in the office where your child was enrolled, either the research room at the Primary Care Center, or Children's Community Pediatrics (CCP) pediatric office, Children's Hospital satellite site or in your home. This visit should take 30 minutes. During this visit, we will ask you how your child is feeling and discuss any concerns you may have. We will get a little bit of mucus from the back of your child's nose at every other visit (every four months) with a flexible swab. The results of the nose culture may help us understand which germs are in the back of your child's nose and knowing this information may help us to figure out which children are more likely to benefit from having ear tubes or more likely to develop bacteria that are resistant to antibiotics. We will also use this swab to look for other things that may predict which children do better.

We would also like to see your child anytime you feel he/she may have a new respiratory illness or symptoms of an ear infection for a sick visit. A general physical exam will be done. We would like to take a picture of the eardrum any time that your child is sick. Sometimes, earwax may need to be removed. You can call us on the study cell phone anytime (412-999-3277). We will arrange a study visit within two days. If your child has an ear infection he/she will be treated as we would normally treat an ear infection with a prescription for standard oral antibiotics or antibiotic ear drops. The treatment is not part of the study. If your child has ear tubes and there is drainage from the ear tube, we would like to use a swab to obtain this material to send for culture to look for bacteria. This visit should take about 30 minutes. If your child had an ear infection at the sick visit, we will treat her with a prescription for antibiotics. We will ask you to complete a short form about your child's symptoms about 5 days after the sick visit. If your phone cannot receive email, we will call you about the symptoms. The phone call will not take more than 10 minutes. We will continue to follow your child for two years after enrollment in this part of the study. Here is a summary of the visits:

Randomization - Enrollment visit

1. At this visit we will describe the purpose of the study to the parent(s) and the randomization process; tympanostomy tube placement vs. non-surgical management.
2. The participant will be randomized
3. If the patient is randomized to get tympanostomy tubes then schedule a visit to the ear, nose, and throat specialist to discuss the surgery within next two weeks. Tympanostomy tubes will be inserted under general anesthesia. Standard of care surgical pre-operative preparation and follow-up will be provided. This procedure is done as clinically indicated and is not a research procedure.
4. Obtain a swab of the nose/throat

Sick visit(s)

1. A child will be seen due to new, continuing or worsening symptoms (clinical decision or parent request).
2. Prescribe antibiotics as necessary for ear infections – standard care, not research
   - oral antibiotics if no tubes
   - ear drops if tympanostomy tubes in place
3. If there is drainage from the ear tube, we will obtain a swab of the fluid to send for microbiology culture
4. If the child has a diagnosis of AOM, a swab of the nose/throat will be obtained.

Email follow-up after ear infection diagnosis

1. Email at days 1- 5
2. Phone call if parent's phone does not accept email
3. Assess if patient needs to be seen again if not improving

Phone call follow-up after ear infection diagnosis

1. A phone call will be made on day 12 after the infection
2. Assess if patient needs to be seen again if not improving

Scheduled follow-up visits

1. Every 8 weeks for 2 years, a total of 8 visits after randomization visit
2. Every other visit a culture of the nose/throat is obtained
3. Every other visit we will do a quality of life assessment
4. At least one visit we will document normal ear examination with digital photo

End of study visit

1. Nose/throat swab for culture
2. Quality of life assessment
3. Parent satisfaction
4. Caregiver impact questionnaire

What are the benefits and risks of participating in this research study?

Risks

Randomization for ear tube placement

Ear tube placement has the potential risks of anesthesia, especially before age 3 years, and of the development, following surgery, of drainage from the tube, blockage of the tube or the tube may come

out on its own. The eardrum can become scarred or develop a hole that remains and does not close back over on its own when the tube eventually comes out.

Randomization for not having ear tubes placed
Any episodes of ear infection would be treated with oral antibiotics. Antibiotic treatment can be associated with diarrhea, diaper rash, or yeast infections. In rare instances, a child may have an allergic reaction to an antibiotic. Some children may have repeated episodes of fluid in the middle ear. In addition, there is potential to cause bacteria to become resistant to the antibiotics.

Nose Swab
A nose swab to test for bacteria in your child's nose will be done. This can commonly (10-25%) cause minor discomfort, mild irritation or possible gagging.

Ear Wax Removal
It may be necessary to remove earwax in order to see the ear drum or take a picture. This can infrequently cause a red area or irritation in the ear canal or minor bleeding. The physician or nurse practitioner looking at your child's ears has had expert training.

Examination and digital image of the ear drum
The risks are those associated with performing an ear examination and obtaining photos of the ear. Some children are uncomfortable holding still for the examination.

Confidentiality
Rarely (<1%), there is a risk of loss of confidentiality. All of the study data will be stored in locked file cabinets that are kept in the research area and computer records are password protected. Electronic data entries will be stored on a secure server that requires an account with a password in order to obtain access. Each computer has a password only available to the study staff. All specimens and electronic symptom questions will only have the patient study identification number on them. Identifying codes that could be used to link your child with this identification number will be kept in a locked file cabinet in the research office.

Internet Communication
Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study.

Benefits
In this study, all children have the potential for benefit. Some of the children will have ear tubes placed which has the benefit of avoiding the use of oral antibiotics and their side effects. The other children who do not have surgery will have the benefit by avoiding surgery and the risk of anesthesia and possible complications of the surgery such as scarring of the eardrum. All study participants will benefit from early detection and appropriate antibiotic treatment of any ear infections that occurs during their participation. All children will have the benefit of close clinician monitoring of their symptoms. If your child is sick or is worsening or not improving as expected, they can be evaluated without delay and treated as needed. You will have 24-hour access to the study physicians who will arrange a study visit, usually within 24 hours, if indicated. This investigation will provide benefit to children who experience recurrent ear infections because this study will help us to determine which

children may benefit from having tubes placed in the ears.

May I refuse to give my permission for the use of my child's medical information for the purpose of this research study?
Your permission to use and share your child's medical information for the purpose of this research study is completely up to you. However, if you do not provide your permission, your child will not be allowed to be in this study.

What alternatives are available to my child if I don't give my permission for him/her to participate in this study?
You may choose not to be a part of the study and have usual clinical care as determined by your health care provider. Participation in this study is up to you. Choosing not to participate in this study will not affect you or your child's present or future relationship with the Children's Hospital of Pittsburgh or any UPMC hospital or affiliated health care provider of the University of Pittsburgh.

What if my child's doctor is one of the investigators for this research study?
If your child's doctor is an investigator in this research study, he/she will be interested both in your child's medical care and in the conduct of this research. Before putting your child in this study or at any time during the study, you may discuss your child's care with your child's pediatrician or family doctor, another doctor at that practice, or a physician or health care provider who is in no way associated with this research project. It is entirely up to you whether to let your child be in any research study offered by your child's doctor.

Do any of the investigators on this study have any other conflicts of interest?
This study is supported by the National Institute of Deafness and Other Communication Disorders, which is part of the National Institutes of Health (NIH). Investigators in the study do not receive individual compensation from your child's participation in this study.

What if there is new information while my child is in this study?
If any information is learned that might affect your willingness to have your child continue to be in this study, you will be informed.

What costs will be associated with permitting my child to participate in this research?
You will not be charged for any study visits or study (research) procedures (nose/throat swabs/cultures) or study visits while your child is a participant in this study. If your child has ear tubes placed the surgery will be standard care and the cost will not be covered by the research study. If your child has ear infections and needs prescriptions to treat the infections, the cost of the medication will not be covered by the research study. If your child develops a yeast diaper rash, we will prescribe an antifungal cream, but the medication is not covered by the research study. You or your insurance company will be charged for surgery or medications and any procedures or treatment performed for your child's routine medical care.

To help cover any expenses such as transportation or time off from work, we will provide a WePay debit card: $25 at randomization visit; $25 for any sick visit or follow-up visit.

How will my child's privacy rights be protected?
Under the Health Insurance Portability and Accountability Act (HIPAA), your child's private health

care information cannot be used for the research purposes of this study without your permission. You will be informed of the specific uses and disclosures of your child's medical information for the purpose of this research study and who will have access to your child's health information.

What uses of my child's medical information will this research involve?
This research study will involve the recording of existing medical information as well as medical information that will become available while your child participates in this study from your child's hospital and/or physician records. From this material, case report forms will be prepared so that your child's medical information, such as prior treatments, medical history and diagnosis can be compared to that of other children participating in this research. These forms will be analyzed by the investigators; the information on the form will not contain any information identifying your child. If the results of this study are published, information concerning your child will be in a form such that he/she cannot be identified.

During your child's participation in this clinical study, the study staff will collect your child's age, gender (male or female), medical history and information on the health and ethnic origin of your child. This information will be reported to the NIH. We will store and process the information about your child using a computer. Your child's personal identity (name, address, and other identifiers) will remain confidential. In the database, your child will only be referred to by a study identification number and initials. Only the study staff will be able to link the code number to your child's name. The NIH or regulatory authorities may directly access your child's medical records in order to determine the accuracy of the reported data. These representatives will observe professional secrecy and keep your child's identity confidential to the extent permitted by law.

Will participation in this research result in medical information being placed in my child's medical records?
Your child's participation in this study will not result in specific research related health information being placed in the Children's Hospital of Pittsburgh medical chart, outpatient chart, or research record. A letter will be sent to your child's primary care provider with information about their study participation and the letter may be added to your medical records. It will include a phone number for your care provider to contact the study if needed.

Who will have access to my child's medical information related to his/her participation in this research study?
In general, research records are kept confidential. Each computer has a password only available to the study staff. Paper records are stored in locked cabinets and computerized records are password protected. There are, however, some disclosures of your child's research-related medical information that may occur. In addition to the investigators listed on the first page of this authorization form and their research staff, the following persons may have access to your child's identifiable private health information related to your child's participation in this research study.

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your child's identifiable medical information) related to your participation in this research study for the purposes of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g. laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your child's identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study. Authorized representatives of the NIH and the Office for Human Research Protections (OHRP) may review and/or obtain your child's identifiable medical information for the purpose of monitoring the accuracy and completeness of the research data, for performing required scientific analyses of the research data, and reanalysis of the research data at a later date and to be sure that the research is being conducted according to the guidelines of each institution. While these organizations have provided their assurance that they will not release your child's identifiable medical information to anyone else, the Children's Hospital of Pittsburgh cannot guarantee this. In unusual cases, the investigators may be required to release your child's research information in response to a court order. Research investigators may be required under Pennsylvania law to report any suspicion of child abuse to child protection services. If the investigators learn that you or someone with whom you are involved is in serious danger of potential severe harm, they may need to warn those who are in danger and contact other agencies to ensure safety.

May I have access to my child's medical information resulting from participation in this research study?

In accordance with the Children's Hospital of Pittsburgh's Notice of Privacy Practices document which you have been provided, you are allowed to look at information (including information resulting from your child's participation in this research study) contained within your child's medical records unless specifically stated.

May I stop my child's participation in this study and may I withdraw my permission for the use of my child's medical information for the purpose of this research study?

You have the right to stop your child's participation in this study at any time. Your child's participation in the study may also be discontinued without your consent, by your doctor, the NIH or the Office for Human Research Protections, if based on their judgment it might improve your child's medical care or if you fail to follow the study schedule. Your child will receive the same quality of care at this hospital whether or not he/she is in the study. Additionally, you may withdraw, at any time, your permission for the use of your child's medical information for the purpose of this research study. Of course, if you withdraw your permission for the use of your child's health information, your child may no longer participate in this research study. To the extent that researchers have already used your child's health information in data analysis and/or scientific publication, this information cannot be withdrawn. Any publication of information will be such that your child's information will not be identifiable. If you decide to withdraw your permission, you should notify your child's study doctor in writing along with the date of your decision. Your decision to withdraw your permission for the use of your child's private health information for this research study will have no effect on your or your child's current or future medical care at Children's Hospital of Pittsburgh, UPMC or affiliated health provider, or the University of Pittsburgh.

For how long will the investigators be permitted to use my child's identifiable health information?

Dr. Hoberman and his study staff will be permitted to use your child's identifiable health information indefinitely. Any information shared with those who are not members of the research team will be in coded, de-identified form.

Will there be any compensation if my child is injured or becomes ill as a result of participating in this study?

If you believe that the research procedures have resulted in an injury to your child, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your child's insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

Could I be contacted for future research studies?

As a parent, the investigators may contact you in the future if we have new research studies that your child may be eligible to participate in. You are under no obligation to participate in future research studies.

Voluntary Consent and Authorization

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions which I have about my child's rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668). Dr. Hoberman 412-999-3277 will be available for questions about this research, my child's rights, and any possible research-related injury. I will receive a signed copy of this consent form.

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Printed Name of Child (Research Subject)

"I understand that, as a minor (age less than 18 years), the above named child is not permitted to participate in this research study without my consent. Therefore, by signing this from I give my consent for his her participation in this research study"

_____ _____

Parent's Name (print) Relationship to Participant (Child)

_____ _____

Parent's Signature Date

Certification of Informed Consent

I certify that I have explained the nature and purpose of this research study to the above-named individual and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about the study have been answered and we will always be available to address future questions as they arise. I further certify that no component of this protocol was begun until after this consent form was signed.

_____ _____

Signature of Investigator Date

_____ _____

Printed Name of Investigator Role in Research Study