Increased Lung Volume as Rescue Therapy for Asthma

NCT02696980

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Informed Consent

Title of Research Project:	Increased Lung Volume as Rescue Therapy for Asthma
Principal Investigator:	Anne E. Dixon, MA, BM, BCh Jason Bates, PhD, DSc
Sponsor:	National Institutes of Health
CHRMS:	16-060

You are being invited to take part in this research study because you have asthma and a body mass index (BMI) of 30 or more. This study is being conducted by the University of Vermont at the UVM Medical Center.

We encourage you to ask questions and take the opportunity to discuss the study with anybody you think can help you make this decision.

Key Information to Help You Decide Whether or Not This Study is Right for You

- This is a research study to learn more about people who gain weight and develop asthma. We are interested in testing if we can help fix asthma symptoms by having people breathe on a machine that makes it slightly harder to breathe out.
- Participants will undergo 5-6 visits:
  - Screening Visit: we will determine if you qualify for the study. This visit includes a blood draw and measurement of height and weight. This visit takes about 1 hour.
  - Visit 1: we will ask about your medical history and ask you to fill out some questionnaires. We will also test your lung function using different machines, and take some measurements of your body. This visit takes about 3 hours.
  - Visit 2: this visit will involve taking pictures of your lungs with CT scans. We will also do a breathing test to test your lung function. This visit takes about 3 hours.
  - Visits 3-5: these visits involve a breathing test where you breathe on a machine that makes it slightly harder to breathe out. These visit take about 1 hour.
  - Additional Visit: an additional visit may be required to repeat some of the breathing tests if necessary.
- There are risks to this study that are described in this document. Some risks include: soreness, lightheadedness, and breathing difficulty from breathing tests, radiation risk from CT imaging, and loss of confidentiality.
- This study is voluntary, and you can stop at any time.

The information above is only a brief summary of the study. If you are interested in learning more, it is important to read the following pages for additional detailed information about the

study. If you decide to take part in the research, you will be asked to provide written consent at the end of this document.

Why is This Research Study Being Conducted?

This research is being conducted to investigate whether we can prevent or reverse airway narrowing in people who gain weight and develop asthma by getting them to breathe out against a slight resistance. This might lead to a new therapy for this type of asthma.

How Many People Will Take Part In The Study?

Twenty people will take part in this study.

What Is Involved In The Study?

This study involves five or six visits over 4-8 weeks, depending on whether the screening visit is required. In addition, you may be asked to return for an additional follow up visit if we need to repeat any of the lung function testing.

Screening Visit (estimated time 45 minutes)

You will be asked to attend a preliminary visit to assess whether you are interested and eligible to participate in the study. We will ask you to attend this visit if we need to draw blood to assess whether or not you are eligible. At this visit we will explain the study to you, and, if you are interested in participating, you will sign this consent form. We will then perform a blood draw for analysis of substances in your blood that cause asthmatic inflammation – we will need approximately 10 cc (2 teaspoons) of blood. In addition, we will review the eligibility criteria for the study with you to make sure you can be in the study. This may involve measuring your height and weight.

Visit 1-5 (estimated time: 3 hours each visit)

1. Medical History:

   We will document your medical history by asking you questions about your past and present health status, medical and surgical history, use of medications, and your family history. We will also be measuring your height, weight, waist circumference and hip circumference, blood pressure, and temperature. We will review medical records of any prior lung function tests and allergy tests.

2. Blood Draw:

   We will draw 16cc (about 4 teaspoons) of blood to measure circulating biomarkers of inflammation.

3. Urine Pregnancy Test:

   If you are a female of childbearing potential, you will be asked to provide a urine specimen to test for pregnancy prior to each methacholine challenge test.

4. Spirometry:

   You will be asked to perform a breathing test called spirometry. This test tells us how well your lungs work. We will need you to take a deep breath in and blow out into a machine as forcefully as you can. This procedure will be repeated a number of times to get good results.

5. Body Plethysmography (Lung Volumes Test)

   This test will be done to measure the volume and airway resistance in the lungs. This involves breathing while sitting in a closed plexiglass box. The box is specifically designed to be as transparent as possible, and the participant and research coordinator can see each other at all times. Participants may open the door at any time from within the box if they feel uncomfortable. The entire test takes less than one minute to complete, this procedure will be repeated a number of times to get good results and takes approximately 5-10 minutes.

6. Single Breath Nitrogen Washout

   This test tells us when the airways in your lungs start to close. You will be asked to take a deep breath of 100% oxygen, and we will measure changes in the concentrations of gases as you breathe out slowly. This procedure will be repeated a number of times to get good results and takes approximately 10-20 minutes.

7. Multiple Breath Nitrogen Washout

   This test tells us about the region of your airways that close while you breathe. You will be asked to breathe normally while breathing 100% oxygen, and we will measure changes in the concentration of gases as you breathe out. This procedure will be repeated a number of times to get good results and takes approximately 10-20 minutes.

8. Standard Methacholine Challenge:

   This test will measure your airway hyper-responsiveness. Methacholine is a drug that can cause the muscles around your airways to constrict, or tighten. You will inhale various concentrations of methacholine through a nebulizer. A nebulizer is a hand held device that aerosolizes the methacholine so you can breathe it in. We will measure how well you can forcibly breathe out air during this test, and how narrow your airways are. A bronchodilator (albuterol) will be given if needed to reverse any remaining constriction. Bronchodilators are inhaled medicines that relax the muscles around your airways. You will not need to do this test if you have had a similar test in the previous 2 weeks.

9. Chest CT:

   Computed tomography (CT scan) at visit 2 only: This is a routine imaging procedure used in pulmonary medicine. We will do 4 scans: one when you take a deep breath in, one when you relax and breathe out, one when you breathe out as far as you can, and a final scan while you breathe out against a small amount of pressure (called positive expiratory pressure, or PEEP).

10. Forced Oscillation Technique (FOT) Methacholine Challenge:

You will inhale one dose of methacholine through a nebulizer like in visit 1. Instead of measuring how forcibly you breathe out air, we will measure how air is moving and how narrow your airways are by having you breathe on a machine that generates little pulses of air, called forced oscillation. We will also ask you to breathe out against a small level of resistance at some of these visits, to see if this changes the way your airways respond to the methacholine. A bronchodilator will be given if needed to reverse any remaining constriction.

Additional Follow up Visit

This visit may be needed if we need to repeat any of the lung function tests. It may include a urine pregnancy test, spirometry, lung volumes, single breath nitrogen washout, multiple breath nitrogen washout, a standard methacholine challenge, or the forced oscillation technique with a single dose of methacholine.

If you have participated in the following study, "Airway Compliance in Relation to BMI in Asthma CHRMS 15-327", or "Increased Lung Volume as Controller Therapy for Asthma CHRMS 16-061", you will not be required to repeat the following procedures for this study: chest CT, lung volumes, and nitrogen washout tests.

Table of Events	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Informed Consent	*				
Baseline Medical History	*				
Venipuncture For Serum Biomarkers	*				
Interim Medical History		*	*	*	*
Asthma Questionnaire	*	*	*	*	*
Berlin Sleep Questionnaire	*				
Pregnancy Test	*	*	*	*	*
CT Imaging		*			
Lung function tests	*	*	*	*	*
Methacholine Challenge	*				
Methacholine with Forced Oscillation and PEEP		*	*	*	*

What Are The Risks and Discomforts Of The Study?

The risks and discomforts that you may experience while participating in this research are as follows:

Blood draw: Having blood drawn can cause some discomfort and there is risk of bruising, infection, redness or swelling at the site where the needle is inserted.

Spirometry, Lung Volumes: There are no known risks to these tests. After this testing some people may have some mild chest soreness from forceful breathing. Since part of this testing involves breathing while sitting in a closed plexiglass box, some participants may feel claustrophobic. The box is specifically designed to be as transparent as possible, and the participant and research coordinator can see each other at all times. Participants may open the door at any time from within the box if they feel uncomfortable.

Nitrogen washout: There are no known risks to either the single breath or multiple breath nitrogen washout tests. There may be a slight discomfort from taking in a deep breath and letting it out gently.

Methacholine challenge: Methacholine can cause headache, throat irritation, lightheadedness, itching, and in rare cases, breathing difficulties when inhaled. In the unlikely event that you have breathing difficulties, medications and equipment to treat you will be available to ensure the procedure is done safely. Technicians are trained to stop the test immediately if you feel any discomfort or if your lung volume (FEV1) drops by more than 20% from baseline. The safety of methacholine during pregnancy is not known, so if you are a woman who might become pregnant, we will advise you to use contraception while participating in this study, and will perform a urine pregnancy test prior to testing with methacholine.

Bronchodilators: On rare occasions (less than 5% of the time), bronchodilators may cause nervousness, a rapid heartbeat or headache at the doses used in this study. If you develop any of these problems, we will monitor you closely until the problem goes away (typically in 30 minutes). On rare occasions bronchodilators may cause arrhythmias (the heart beats in an abnormal way) or low potassium: these side-effects are usually related to taking high doses of the medication, and so are very unlikely to occur during this study.

Forced oscillation: Measurement of oscillation mechanics using the forced oscillation technique at the mouth has been performed worldwide with no complications. Occasionally, some subjects report a slight discomfort from the small pulses of air that are provided at the mouth, but there are no reports of interference with breathing or any other complications.

Radiation exposure from CT: The scan results in a radiation dose of 4-7 mSv. This is a routine imaging procedure used in pulmonary medicine. We plan to perform limited scans of your lungs. This is equivalent to the exposure from natural background radiation in our surroundings over 1-2 years. For comparison, the maximal permissible whole-body occupational radiation dose set by the federal government for people who work with radiation or volunteer for medical research is 50 mSv per year.

Abnormality detected during study procedures: If an unexpected abnormality on the chest CT, or in lung function testing, we will communicate with your permission, to your primary care physician. If you do not have regular physician, we will help you schedule an appointment with an appropriate health care provider.

Long-term Storage of Samples

We have a number of tests planned for the blood samples and information that we collect from you during this study. We are also hoping to store any leftover blood samples and data you provide for future research on obesity and asthma. We will store your samples and data with a code number, not your name, so laboratory personnel will not be able to identify you. The list connecting your name to this code will be stored separately. If you decide you no longer want your samples and data stored, you should contact Dr. Dixon to let her know and your samples will be destroyed. Participation in this long-term storage of samples is voluntary, and if you choose not to allow it or withdraw later, your participation in the main study will not be affected.

Check the box below and initial alongside if you give permission for left-over samples and data to be used stored/disclosed/shared for future research projects.

☐ _____ (initials)

What Are The Benefits of Participating In The Study?

Taking part in this research study will not benefit you personally. However, by participating in this study we may learn new information that will help patients in the future who have lung diseases.

What Other Options Are There?

The only option is to not participate in this study. The decision to not participate will not affect the care you receive.

Are There Any Costs?

The only cost to you for participating in this study is your time.

What Is the Compensation?

If you qualify for the study, you will be compensated $100 for completion of each ofVisits 1-5. If you undergo a chest CT at visit 2, you will receive an extra $50. You will not be compensated for the screening visit. Compensation for completion of all study visits will be up to $550 total. If an additional follow up visit is required to repeat lung function testing, you will be compensated an extra $50.

In addition if you drive 40 or more miles round trip from your home to the Vermont Lung Center, you will receive payment for mileage at standard UVM rates.

Can You Withdraw or Be Withdrawn From This Study?

Your participation in this research study is voluntary. You may decline to participate or you may withdraw at any time without prejudice, penalty or loss of benefits to which you are entitled.

If you cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Any information collected up to the point you wish to stop your participation will be used for research purposes.

The investigator may end your participation in this study without your consent for any of the following reasons:

- It is not in your best medical interests to continue
- You need treatment not allowed in this study
- You cancel permission to disclose your health information
- You fail to follow instructions, or
- The study is canceled.

What About Confidentiality of Your Health Information?

What health information will be used and disclosed for this study?
The health information we plan to collect for this study is listed below.

- Medical history and examinations
- Information that identifies you, such as your name, address, age, and sex
- Reports from hospital and clinic visits
- Laboratory and other test results
- X-ray and other images and reports
- Lists of medications you are taking
- Responses to health surveys and questionnaires

Who is disclosing your health information for this research study?

- The University of Vermont Medical Center

- Other doctors' offices and hospitals where you may receive medical care while this study is active.

Who will use your health information in this study?
Our research team will use your health information. We may also share it with those who assist with the conduct of the research or oversight of the activities for this study. The representatives from the institutions, organizations, and agencies are listed below.

- The University of Vermont and its Committees on Human Research
- The University of Vermont Medical Center
- The sponsor of this study, the National Institutes of Health, or others who fund the research, including the government
- Other researchers and centers that are a part of this study, including individuals who oversee research at those sites
- Officials from agencies and organizations that provide accreditation and oversight of research
- Federal and state agencies that oversee or review research information, such as the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services, the National Institutes of Health, and public health and safety authorities

Your health information is protected by a federal law called the Health Information Portability and Accountability Act (HIPAA). Once your health information is shared outside of the University of Vermont Medical Center, we cannot guarantee that these laws will continue to apply. As a result, your health information could be further disclosed for other purposes. In the absence of a Certificate of Confidentiality, it is also possible for a court or other government official to order the release of study data. The confidentiality of your health information cannot be guaranteed if you agree it may be used in this study.

Certificate of Confidentiality
This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this certificate may not disclose or us information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable disease but no for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other

person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document including research data in the medical record.

Future Research
Your samples and data will be stored for future use if you have indicated that earlier in this consent form.

How long will your health information be used for research?
Your permission to use your health information will not end until the study is completed. During this study, you will not have access to study data. You may ask for your data once study activities are complete. You have a right to receive a copy of the information in your medical record at any time.

What if you decide not to give permission for research use of your health information?
If you decide not to allow the use and disclosure of your health information, you may not take part in this study. Your decision will have no effect on your current or future medical care.

If you choose to stop taking part in this study in the future, you may cancel permission for the use of your health information. You should let the research team know that you are cancelling your permission. A member of the research team will assist you in making your decision effective. The study will continue to use the health information already collected for the study before you cancelled your permission, and you cannot get back information that was already shared with others.

Who can answer your questions about the use and disclosure of your health information?

If you have questions or concerns about the use and disclosure of your health information, you should ask a member of the study team at (802) 847- 2193 or the Privacy Officer at The University of Vermont Medical Center, Inc. at (802) 847-2667.

Safeguarding Your Health Information

A record of your progress will be kept in a confidential form at the Vermont Lung Center. The security of your record will be maintained by the research team. The results of this study may eventually be published and information may be exchanged between medical investigators, but patient confidentiality will be maintained.

If your record is used or disseminated for government purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency.

You may be requested to provide your name, social security number, and address. This information will be disclosed one time to either the University of Vermont's Procurement Services Department or UVM Medical Center Accounts Payable Department for purposes of reimbursing you for participation in this study. If you are not a US Citizen or Permanent Resident Alien you will be required to complete additional paperwork for payment.

Clinical Trials Registration

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What Happens If You Are Injured?

The UVM Medical Center Policy

If you are injured or become ill as a result of being in this research, the UVM Medical Center, the hospital partner of the University of Vermont, will provide reasonable and usual medical care for that injury or illness. There will be no cost to you if the conditions listed below apply to your injury or illness. These conditions are:

1. The investigator, in consultation with the study sponsor, determines that your injury or illness results from the research and not from your underlying condition or its usual treatment.

2. You let the investigator know about the injury or illness when you first notice it; and

3. You follow medical advice about proper treatment options for the injury or illness.

The UVM Medical Center may claim payments for your medical treatment directly from the study sponsor or your insurance company when these payments are allowed.

For an injury or illness that results from being in this study, the University of Vermont Medical Center will not offer you any other payments, such as lost wages or expenses, except for your medical care. Even though you may receive medical care at no cost to you under certain conditions if you are in this study, the UVM medical center and the University of Vermont do not admit to any responsibility for an injury or illness that results from being in the study.

If you agree to take part in this study and you sign this consent form, you are not giving up any of your legal rights.

Contact Information

You may contact Dr. Dixon, the Investigator in charge of this study, at 802- 847-1158 for more information about this study. If you have any questions about your rights as a

participant in a research project or for more information on how to proceed should you believe that you have been injured as a result of your participation in this study you should contact the Director of the Research Protections Office at the University of Vermont at 802-656-5040.

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Statement of Consent

You have been given and have read or have had read to you a summary of this research study. Should you have any further questions about the research, you may contact the person conducting the study at the address and telephone number given below. Your participation is voluntary and you may refuse to participate or withdraw at any time without penalty or prejudice to your present and/or future care.

You agree to participate in this study and you understand that you will receive a signed copy of this form.

_____

Signature of Subject Date

This form is valid only if the Committees on Human Research's current stamp of approval is shown below.

_____

Name of Subject Printed

_____

Signature of Principal Investigator or Designee Date

_____

Name of Principal Investigator or Designee Printed

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