

# Allergen-Impermeable Bed Covers for Adults with Moderate to Severe Asthma and Dust Mite Allergy

*Judy Nam*

## A. Study Purpose and Rationale

The number of persons in the United States reported to have asthma doubled between 1980 and 1996, then reached a plateau (Manino, 2002). In 2001, the Center for Disease control estimated that 20.3 million people had asthma (CDC, 2001). Asthma remains a growing concern in this country, particularly in inner-city African-American and Latino populations. While the management of asthma has improved over the past two decades, these inner-city populations showed increased rates of morbidity and mortality from asthma. African-Americans and Hispanic Americans are two to six times more likely to die from asthma than whites (Lenoir, 1999). In addition to socioeconomic issues and access to healthcare, there have been many theories put forward to explain this finding. Current theories include: exposures to allergens, pollutants and infections.

Exposure of asthma patients to irritants or allergens to which they are sensitive has been shown to increase asthma symptoms and precipitate asthma exacerbations (Cockcroft, 1979). The National Asthma Education and Prevention Program recommends that those patients with persistent asthma on daily medications should be assessed for exposure and allergy to indoor perennial allergens, such as dust mite (1997). For patients with persistent asthma found to have dust mite sensitization, this panel of experts sites allergen avoidance as the most important step in the treatment. Because the bed is the most important source of dust mite exposure (Platts-Mills, 1982), the current strongest recommendations to control dust mite exposure are: encasing mattresses and bedding in an allergen-impermeable covers, and to wash bedding in hot water weekly.

Although many studies have documented a decrease in mite allergen 6 or more months following a range of interventions, it remains unclear if allergen avoidance results in a clinical benefit (Woodcock, et al., 2003; Cloosterman, et al., 1999). It has been a challenge to establish whether effective allergen avoidance can be achieved through measures that are practical and cost effective and flexible enough to suit individual needs, and to determine which patients may benefit from such interventions.

This study will address whether dust mite allergen avoidance through allergen-impermeable mattress covers and bedding covers will have a clinical benefit on patients with persistent asthma and dust mite allergy.

## B. Study Design and Statistical Analysis

### a. Study Arms

All eligible subjects will proceed in a 4 week run-in phase, during which they will complete a diary card documenting beta<sub>2</sub>-agonist use, morning peak expiratory flow rate (record the best-of-3 efforts [Mini-Wright flowmeter, Clement Clarke International], scores for daytime and nighttime symptoms. Those who complete the diary cards for at least 14 days will undergo stratification as moderate or severe persistent asthma by this information, then randomly assigned to receive allergen-impermeable or placebo bedding. At randomization, they will undergo complete detailed questionnaire regarding demographics, medication use, smoking exposure, time spent away from home, occupational exposures. They will also be administered the St. George Hospital Respiratory Questionnaire to assess quality of life.

The active intervention arm and the placebo arm will be asked to keep covers on their beds and bedding for one year.

### b. Number of subjects to be enrolled / Methods of Statistical Analysis

Number of subjects to be enrolled in each arm = 191 subjects

This was determined by the unpaired t-test, using:

- mean of the placebo arm (frequency of beta<sub>2</sub>-agonist use) as 4 puffs/day
- mean of the active intervention arm as 3 puffs/day
- standard deviation = 3 puffs/day
- effect = 1 puff/day
- alpha = 0.05
- power = 0.90

**c. Randomization**

Patients will be stratified as moderate or severe asthmatic prior to randomization to achieve equal numbers of each in both arms.

**C. Study Procedure**

There will be a 2 year enrollment period. Each subject will participate for one year plus a one month run-in period.

**a. Allergy testing**

According to the National Asthma Education and Prevention Program, the patients eligible to participate in this study have indications for allergy testing. Skin prick testing will be performed once at the beginning of the study. This test is slightly uncomfortable, but is usually well tolerated and accurate, even in small children and infants. Local itch and swelling normally subsides within 1-2 hours. More prolonged or severe swelling may be treated with an oral antihistamine, topical corticosteroid cream and an ice pack. Occasional patients will experience feel dizzy or light-headed and need to lie down. Severe allergic reactions from allergy testing in asthma are very rare, and can be avoided by not testing patients during an asthma exacerbation. An allergist will administer the test and observe the patient for 1 hour after the procedure for any adverse reactions.

**b. Dust Collection**

The patient's home will be visited to collect dust at the beginning of the study, at 6 months, and at 12 months. Dust mite allergen on the patient's bed will be collected by vacuuming of a 1 m<sup>2</sup> area of the mattress for 2 minutes through a filter device. The samples will be assayed by monoclonal enzyme-linked immunosorbent assay for dust mite allergen, *Der p 1* (Indoor Biotechnologies) (microgram allergen/gram of dust).

Patients will be asked to record the best of 3 Peak Expiratory Flow Rate (PEFR) daily for a total of 12 weeks through the year (increments of 4 weeks at a time). Patients will each be given a peak expiratory flow meter, a small hand-held device with a mouthpiece at one end and a scale with a moveable indicator (usually a small plastic arrow). Asthmatic patients will be familiar with the method, but will be instructed to proper use of the device. (They will be instructed to breathe in as deeply as possible, then blow into the instrument's mouthpiece as hard and fast as possible.)

**D. Study Drug**

N/A

**E. Medical Device**

Allergen-impermeable microfiber covers (Allergy Control Products) is a commercially available device which retain >99.5% of 0.4micrometer particles. (Dust mite allergens are about 10 micrometer particles.) The sham covers will be of the same material but of a conventional weave allowing 85% of

allergen to pass through. The patients will be asked to use the covers on their beds, pillows, blankets or duvets for the duration of the study, one year.

## F. Study Questionnaires

Patients will be assessed with questionnaire, a 4-week diary of symptoms (see attached.) and 4-diary of daily morning best-of-3 peak expiratory flow rates. These evaluations will occur at the beginning of the study, at 6 months, and at 12 months. They will also be asked about the number of emergency department visits and unscheduled physician visits for asthma exacerbations, as well as frequency of systems steroid use in the previous 6 months period. Patients will receive a reminder phone call at months 5 and 11 to commence with the 4-week diary.

## G. Study Subjects

### a. Inclusion Criteria

- moderate persistent or severe persistent asthma \*
- positive skin test to dust mite (at 15 minutes, wheal equal to or greater than positive control, histamine)
- ages 18-50 yrs
- resident of upper Manhattan
- The National Asthma Education and Prevention Program defines:

Moderate Persistent Asthma as	
<i>symptom:</i>	daily symptoms
	daily use of inhaled short-acting beta <sub>2</sub> -agonist
	exacerbations affect activity
	exacerbations ≥ 2/week, may last days
<i>nighttime symptoms:</i>	>1/week
<i>lung function:</i>	FEV1 or PEFr >60% to <80% predicted
Severe Persistent Asthma as	
<i>symptoms:</i>	Continual symptoms
	Limited physical activity
	Frequent exacerbations
<i>nighttime symptoms:</i>	Frequent
<i>lung function:</i>	FEV1 or PEFr ≤ 60% predicted

### b. Exclusion Criteria

chronic systemic steroid use

- underlying chronic lung disease other than asthma
- current allergen-impermeable bed cover use
- diagnosis of CHF
- pet owner and sensitization to their pet by skin test
- pregnant
- more than one bed in the bedroom

This study is not restricted by race or gender.

No vulnerable populations will be included in this study.

## H. Recruitment of Subjects

Physicians practicing in Pulmonary, Allergy, General Medicine, Asthma clinics in upper Manhattan will give study description and will agree that the patient is suitable for the study. The patient's physician will ascertain if the patient is willing to discuss the study with the research team. Patients will be invited by phone call to discuss the study. After obtaining consent, those who qualify will be seen by an allergist who will administer the allergy skin prick test to dust mite. Those with a dog and/or cat will also be skin tested to dog and/or cat. Those found to have sensitization to dust mite allergen and not sensitized to their pet will commence with the study.

#### **I. Confidentiality of Study Data**

After randomization, the patient's initials, date of birth, and measurements for his/her bed/bedding will be sent to the ICCR. Each patient will be assigned a research number. The bedding measurements will be sent by the ICCR to the manufacturer of the covers who will mail the boxes to the research center with only the research number as an identifier.

Data will be stored so that only researchers can access the information.

#### **J. Potential Conflict of Interest**

Neither the investigators nor the University has any proprietary interest in the study device.

#### **K. Location of Study**

The intervention or placebo will take place in patients' homes in upper Manhattan. The intervention does not involve risk to the subjects.

Allergy testing and interviewing will take place at ICCR.

#### **L. Potential Risks**

The intervention, allergen-impermeable cover, is well tolerated. Previously studies utilizing these products have not reported any adverse reaction or worsening of asthma.

#### **M. Potential Benefits**

Patients may have improved asthma symptoms and quality of life.

#### **N. Alternative Therapies**

The proposed intervention is not experimental. Allergen impermeable covers are recommended by The National Asthma Education and Prevention Program and are currently routinely prescribed by physicians taking care of dust-mite allergen sensitized patients.

#### **O. Compensation to Subjects**

Patients will be compensated for any expenses incurred while traveling to and from CUMC.

At the end of the study, all subjects in the placebo arm will receive allergen-impermeable covers for their beds.

#### **P. Cost to Subjects**

None.

**Q. Minors as Research Subjects.**

N/A

**R. Radiation or Radioactive Substances**

N/A

**S. References**

CDC, National Center for Health Statistics. Asthma prevalence, health care use and mortality, 2000-2001.

Cockcroft DW, et al. Determinants of allergen-induced asthma: dose of allergen, circulating IgE antibody concentration, and bronchial responsiveness to inhaled histamine. *Am Rev Respir Dis*, 1979 Nov;120(5):1053-8.

Cloosterman SGM, Shermer TRJ, et al. Effects of house dust mite avoidance measures on Der p 1 concentrations and clinical condition of mild adult house dust mite-allergic asthmatic patients, using no inhaled steroids. *Clin Exp Allergy*, 1999;29:1336-1346.

Lenoir MA. Asthma in inner cities. *J Natl Med Assoc*.1999 Aug;91(8 Suppl):1S-8S.

Mannino DM, Homa DM, Akinbami LJ, et al. Surveillance for asthma---United States, 1980--1999. In: CDC surveillance summaries (March 29). *MMWR* 2002;51(No. SS-1).

National Asthma Education and Prevention Program Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma, NIH Publication No. 97-4051, 1997.

Platts-Mills TAE, Tovey ER, Mitchell EB, et al. Reduction of bronchial hyperreactivity during prolonged allergen avoidance. *Lancet* 1982;2:675-8).

Woodcock, A, Forster, L, Matthew, E, et al. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. *N Engl J med* 2003;349:225-236.

Barr JT, Schumacher GE, Freeman S, LeMassie M, Balas AW, Jones PW. American Thoracic Society. Modification and Validation of the St. George's Respiratory Questionnaire. *Clinical Therapeutics* 2000; 22:1111-1145.

The St. George's Hospital Respiratory Questionnaire  
 This questionnaire is designed to help us learn more about how your breathing is troubling you and how it affects your life. We are using it to find out which aspects of your illness cause you the most problems, rather than what the doctors and nurses think your problems are. Please read the instructions carefully and ask if you do not understand anything. Do not spend a long time deciding on your answers.

**PART 1 - Four Week Description**

Please describe how often your lung/respiratory problems have affected you over the last four weeks. Please fill in one circle for each question.

- |  |                  |                     |                    |                                       |            |
|--|------------------|---------------------|--------------------|---------------------------------------|------------|
|  | almost every day | several days a week | a few days a month | only with lung/respiratory infections | not at all |
|--|------------------|---------------------|--------------------|---------------------------------------|------------|
- Over the last 4 weeks, I have coughed
  - Over the 4 weeks, I have brought up phlegm (sputum)
  - Over the last 4 weeks, I have had shortness of breath
  - Over the last 4 weeks, I have had episodes of wheezing
  - During the last 4 weeks, how many severe or very unpleasant episodes of lung/respiratory problems have you had?
 

more than 3 episodes	<input type="radio"/>
3 episodes	<input type="radio"/>
2 episodes	<input type="radio"/>
1 episode	<input type="radio"/>
No episodes	<input type="radio"/>
  - How long did the worst episode of lung/respiratory problem last?
 

a week or more	<input type="radio"/>
3 or more days	<input type="radio"/>
1 or 2 days	<input type="radio"/>

 Go to Question 7 if you didn't have a severe episode.

- I am short of breath when I bend over
- My coughing or breathing disturbs my sleep
- I become exhausted easily

**Section 4:** These are questions about other effects that your lung/respiratory problem may have on you. Please fill in each circle that applies to you now.

- |   |                       |      |       |
|---|-----------------------|------|-------|
| My coughing or breathing is embarrassing in public                            | <input type="radio"/> | True | False |
| My lung/respiratory problem is a nuisance to my family, friends, or neighbors | <input type="radio"/> |      |       |
| I panic or get afraid when I cannot catch my breath                           | <input type="radio"/> |      |       |
| I feel that I am not in control of my lung/respiratory problem                | <input type="radio"/> |      |       |
| I do not expect my lung/respiratory problem to get any better                 | <input type="radio"/> |      |       |
| I have become frail or an invalid because of my lung/respiratory problem      | <input type="radio"/> |      |       |
| Exercise is not safe for me   | <input type="radio"/> |      |       |
| Everything seems too much of an effort  | <input type="radio"/> |      |       |

**Section 5:** These are questions about your lung/respiratory medication, including oxygen, inhalers, and pills. If you are not receiving medication, go to Section 6. Please fill in each circle that applies to you now.

- |  |                       |      |       |
|--|-----------------------|------|-------|
| My lung/respiratory medication does not help me very much          | <input type="radio"/> | True | False |
| I get embarrassed using my lung/respiratory medication in public   | <input type="radio"/> |      |       |
| I have unpleasant side effects from my lung/respiratory medication | <input type="radio"/> |      |       |
| My lung/respiratory medication interferes with my life a lot       | <input type="radio"/> |      |       |

**Section 6:** These are questions about how your activities might be affected by your breathing problem. For each question, answer True if one or more parts applies to you because of your breathing problem. Otherwise answer False.

- |  |                       |      |       |
|--|-----------------------|------|-------|
| I take a long time to get washed or dressed  | <input type="radio"/> | True | False |
| I cannot take a bath or shower, or I take a long time to do it   | <input type="radio"/> |      |       |
| I walk slower than other people my age, or I stop to rest  | <input type="radio"/> |      |       |
| Tasks such as household chores take a long time, or I have to stop to rest   | <input type="radio"/> |      |       |
| If I walk up one flight of stairs, I have to go slowly or stop   | <input type="radio"/> |      |       |
| If I hurry or walk fast, I have to stop or slow down   | <input type="radio"/> |      |       |
| My breathing problem makes it difficult to do things such as walking up hills, carrying things up stairs, light gardening such as weeding, dancing, playing golf, or light sports such as horseshoes | <input type="radio"/> |      |       |
| My breathing problem makes it difficult to do things such as carrying heavy loads, digging in the garden or shoveling snow, jogging or walking briskly, playing tennis, or swimming                  | <input type="radio"/> |      |       |

- less than a day
- 7) Over the last 4 weeks, in an average week, how many good days (with few lung/respiratory problems) have you had?
 

none	<input type="radio"/>
1 or 2	<input type="radio"/>
3 or 4	<input type="radio"/>
nearly every day	<input type="radio"/>
every day	<input type="radio"/>
- 8) If you wheeze, is it worse in the morning?
 

No	<input type="radio"/>
Yes	<input type="radio"/>

 If you don't wheeze, go to the next page.

**Part 2**

**Section 1:** How would you describe your lung/respiratory condition? Please fill in one circle only.

The most important problem I have	<input type="radio"/>
Causes me a lot of problems	<input type="radio"/>
Causes me a few problems	<input type="radio"/>
Causes me no problem	<input type="radio"/>

If you have ever held a job, please fill in one of the circles.

My lung/respiratory problem made me stop my job	<input type="radio"/>
My lung/respiratory problem interferes with my job or made me change my job	<input type="radio"/>
My lung/respiratory problem does not affect my job	<input type="radio"/>

**Section 2:** These are questions about what activities usually make you feel short of breath. Please fill in each circle that applies to you now.

Sitting or lying still	<input type="radio"/>	True	False
Washing yourself or dressing	<input type="radio"/>		
Walking in the house	<input type="radio"/>		
Walking outside on level ground	<input type="radio"/>		
Walking up a flight of stairs	<input type="radio"/>		
Walking up hills	<input type="radio"/>		
Playing sports or active games (baseball, tennis, etc.)	<input type="radio"/>		

**Section 3:** These are more questions about your cough and shortness of breath. Please fill in each circle that applies to you now.

Coughing hurts	<input type="radio"/>	True	False
Coughing makes me tired	<input type="radio"/>		
I am short of breath when I talk	<input type="radio"/>		

My breathing problem makes it difficult to do things such as very heavy manual labor, riding a bike, running, swimming fast, or playing competitive sports

**Section 7:** We would like to know how your breathing usually affects your daily life. Please fill in each circle that applies to you because of your lung/respiratory problem.

- |   |                       |      |       |
|---|-----------------------|------|-------|
| I cannot play sports or active games                    | <input type="radio"/> | True | False |
| I cannot go out for entertainment or recreation         | <input type="radio"/> |      |       |
| I cannot go out of the house to do the grocery shopping | <input type="radio"/> |      |       |
| I cannot do household chores                            | <input type="radio"/> |      |       |
| I cannot move far from my bed or chair                  | <input type="radio"/> |      |       |

Here is a list of other activities that your lung/respiratory problem may prevent you from doing. (You do not have to fill-in these, they are just to remind you of ways in which your shortness of breath may affect you):

- Going for walks or walking the dog
- Doing activities or chores at home or in the garden
- Having sexual intercourse
- Going to church, or a place of entertainment
- Going out in bad weather or into windy rooms
- Visiting family or friends or playing with children

Please write in any other important activities that your lung/respiratory problem may stop you from doing:

Now, would you fill in the circle (only one) that you think best describes how your breathing problem affects you:

- |  |                       |      |       |
|--|-----------------------|------|-------|
| It does not stop me from doing anything I would like to do   | <input type="radio"/> | True | False |
| It stops me from doing one or two things I would like to do  | <input type="radio"/> |      |       |
| It stops me from doing most of the things I would like to do | <input type="radio"/> |      |       |
| It stops me from doing everything I would like to do         | <input type="radio"/> |      |       |

Thank you for completing this questionnaire. Please check to be sure that you have answered all questions.

**Diary Card for Asthma Symptoms**

<b>Parameter</b>	<b>Finding</b>	<b>Score</b>
sleep disturbance	no sleep disturbance due to asthma	0
	awoken once during the night for less than an hour because of asthma	1
	awoken two or three times or once for more than an hour because of asthma	2
	awake most of the night because of asthma	3
chest tightness on awakening	not present and didn't require extra bronchodilator during the night	0
	not present but did require extra bronchodilator during the night	1
	present	2
duration and frequency of daytime wheeze and breathlessness	none	0
	occasional	1
	frequent but not all day	2
	most or all of the day	3
severity of daytime wheeze and breathlessness	none	0
	mild; not incapacitating or distressing	1
	moderate to severe; distressing and/or had to limit activities	2
cough	none	0
	occasional	1
	more than occasional	2