

# Breath of Fresh Air

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Information, news and advice for improving asthma well-being

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## Asthma and Reflux: What's the Link?

A nagging question for patients with poorly controlled asthma and for their doctors is the following: might acid reflux be playing a role in making the asthma difficult to control, and might treatment of acid reflux help to control asthma? New information from a well-done experiment is available to help answer this question.

Nearly everyone has experienced an episode of reflux at least once. We are speaking of the regurgitation of stomach contents—stomach “juices”—from the stomach back up the esophagus (swallowing tube) into the chest. Reflux is typically experienced as a burning sensation behind the breast bone, or the regurgitated liquid may suddenly appear in the back of the throat, bringing with it a bitter or sour taste or the taste of recently eaten food.

A muscle that rings the esophagus at its end where it meets the stomach is meant to tighten, preventing food, stomach acid, and digestive juices from returning back “the wrong way” out of the stomach. However, in some people this muscle sphincter is unusually lax and allows frequent return of stomach contents into the esophagus, particularly when one lies down and gravity no longer helps to keep material in the stomach. Stomach acid that is repeatedly splashed onto the lining of the esophagus can cause serious problems and is considered a disease: gastroesophageal reflux disease or GERD. People with GERD may experience severe chest pain and think that they are having a heart attack. Or they may have a vague sense of tightness in their chest, feeling unable to get a full, satisfying breath, not too dissimilar to an asthma attack. It is even possible to have stomach acid reflux all the way up the esophagus to one's throat, where small amounts can be unknowingly breathed onto the bronchial tubes. You can imag-

ine that aspiration of even tiny amounts of stomach acid onto the breathing tubes will be bad for asthma!

### Silent Reflux

To make matters more complex, it is possible to have acid reflux and not know it. It is said that as many as half the people with reflux may have no symptoms at all, so-called “silent reflux.” If one measures for the regurgitation of stomach acid into the esophagus (using an instrument called a pH probe to record the acidity or pH of the liquid in the esophagus), one finds abnormally frequent reflux of stomach acid occurring in people without any symptoms. How often does this happen in people with asthma? It depends who is doing the testing and in which patients, but anywhere from  $\frac{1}{3}$  to  $\frac{2}{3}$  of asthmatic patients tested had abnormal acid reflux.

It is clear that asthma and acid reflux are both common and interrelated. It is possible for severe and symptomatic GERD to cause asthma to worsen, as well as to cause chest symptoms that feel like one's asthma is acting up. And poorly controlled asthma, along with some of the medicines used to treat it, can cause more frequent reflux. But what is the role of “silent” or minimally symptomatic reflux in causing asthma to worsen? If your asthma is not well-controlled despite appropriate treatment, should you be worried that acid reflux is playing a role, even in the absence of symptoms of heartburn?

That specific question was addressed in a research study recently published in the *New England Journal of Medicine*. Doctors investigated the role of silent or minimally symptomatic reflux in approximately 400 persons whose asthma remained poorly controlled despite taking their controller medication (an inhaled steroid) every day. All of



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## News About Asthma

### Bronchial thermoplasty

A major cause of asthma symptoms is contraction of the muscles that ring the breathing tubes. These muscles, which are not under the control of your conscious brain, can squeeze down on your air passageways, making them so narrow that it becomes difficult to breathe. Allergens, cigarette smoke and other irritants, viral infections, stress, and certain medications can all provoke these muscles to constrict the bronchial tubes.

What would happen if you could weaken these bronchial tube muscles, interfering with their ability to contract around the bronchial tubes? Might you help to prevent asthmatic attacks and reduce asthmatic symptoms? There is no clear benefit from having bronchial muscles that can contract to the extent seen in asthma; one would not predict any harmful effect from weakening these muscles.

Bronchial thermoplasty is the name given to the procedure, done via bronchoscopy, by which heat is applied to the wall of the bronchial tubes in sufficient amounts that the muscles in the walls of the tubes are thinned and weakened. At the recent annual meeting of the American Thoracic Society, the results of a randomized trial of bronchial thermoplasty vs. pretend (sham) thermoplasty were reported. Dr. Michael Wechsler, pulmonologist at the Brigham and Women's Hospital, was a participant in this research. Patients who received the real treatment with bronchial thermoplasty experienced fewer asthmatic attacks, fewer emergency department visits, and fewer days lost from work or school compared with those given pretend treatment. Overall, they were more likely to describe the quality of their lives as significantly improved. The bronchoscopic treatments occasionally caused transient worsening of asthma; no long-term adverse effects have been described as of yet. The FDA is expected to consider the role of bronchial thermoplasty in the treatment of asthma later this year.

### New antihistamine

A new antihistamine tablet has been approved for the treatment of allergies. It is called levocetirizine, with the brand name Xyzal.

“First-generation” antihistamines, such as diphenhydramine (Benadryl) and chlorpheniramine (Chlortrimeton), are often effective for treating itching and other allergic symptoms of the nose and eyes, but they can have unpleasant side effects, such as sleepiness, excessive dryness, and difficulty with urination (in men with large prostate glands). “Second-generation” antihistamines are equally effective but with fewer such side effects. They include loratadine (Claritin), desloratadine (Clarinex), cetirizine (Zyrtec), and fexofenadine (available as generic fexofenadine as well as Allegra). Levocetirizine (Xyzal) is a new, prescription-only, second-generation antihistamine available for once-daily dosing (tablet and liquid formulations, approved for adults and children 6 years and older). Although we all may have our own unique reactions to different medications, *in general* the various second-generation antihistamines are all equally effective with few differences among them. Loratadine and cetirizine are available in drugstores without a prescription.

### Leukotriene blockers and insomnia

For the last several months the FDA has been reviewing potential side effects of the asthma medications called leukotriene blockers or leukotriene modifiers. These include montelukast (Singulair), zafirlukast (Accolade), and zileuton (Zyflo). In the experiments (clinical trials) that led the FDA to approve these medications, side effects were very rare. However, since their approval and widespread use in both adults and children to treat asthma and allergies, reports have surfaced about potential effects of these medications on mood, behavior, and thinking.

Most concerning were reports of suicide or thoughts of committing suicide related to these *continued on page 3*

## Breath of Fresh Air

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medications. The FDA reviewed all available information and concluded that suicide and suicidal thoughts are *not* caused by the leukotriene blockers.

At the same time, reports came to the FDA about agitation, aggression, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, and tremor. Of these, difficulty sleeping was the most common. In June the FDA asked the manufacturers of these three medications to make mention of these potential side effects under the heading of Precautions in their drug labeling information or “package insert.” Next, the drug manufacturers will have an opportunity to respond to this request from the FDA. In the meantime, the FDA continues its review and plans to issue a final report of its investigation in several months.

### **Loss of sense of smell due to Zicam nasal spray**

Who wouldn't like to be able to stop a viral infection at its earliest stages, before it develops into a full-fledged head and chest cold? If only we had a truly effective preventive therapy for the “common cold.” Perhaps you have found something that you feel works for you: lots of vitamin C, Echinacea, the herb and vitamin combination called Airborne, zinc tablets, or gargling with Listerine. The effectiveness of any of these remedies requires a good bit of faith; there is no available scientific evidence to support their usefulness. But is there any harm taking them?

The FDA says, yes, for the zinc-containing nasal remedies called Zicam Cold Remedy Nasal Gel and Zicam Cold Remedy Swabs, there is serious potential harm. Hundreds of people have complained of a loss of their sense of smell after using these products, and their manufacturer, Matrixx Initiatives, has agreed to stop their sale.

### **Bad news for the tobacco industry; good news for lungs**

Persons with asthma are not immune to nicotine addiction. While cigarette smoking is harmful for everyone—it is the number one preventable cause of premature death in this country—its relation to asthma is particularly troubling. Cigarette smoking can predispose to the development of asthma, can make asthma worse,

and can interfere with the effectiveness of medications used to treat asthma.

This Spring the Centers for Disease Control released the latest statistics regarding the frequency with which Americans are still smoking cigarettes. This information comes from a large telephone survey of households throughout the country, conducted in 2007, as part of the annual National Health Information Survey. The results are based on self-reported cigarette smoking habits in persons over age 18 years. Two pieces of information are particularly striking:

For the first time since before World War II, fewer than 20% of American adults are active cigarette smokers. There was a time (1965) when as many as 42% of American adults smoked cigarettes, including more than half of all adult men. Now, the prevalence of cigarette smoking among men is 22.3% and among women 17.4%.

More persons with a history of prior cigarette smoking have quit smoking than continue to smoke. In America former smokers outnumber current smokers.

Another cause for optimism regarding the gradual demise of cigarette smoking addiction in the United States is the Family Smoking Prevention and Tobacco Control Act, which was signed into law by President Obama on June 22. This law now gives the Food and Drug Administration the ability to regulate the tobacco industry. According to the on-line group, Consumerism Commentary, the primary focus of the law is an effort to stop cigarette manufacturers from aggressively marketing their products to children. To this end, it will be illegal to sell candy-flavored and fruit-flavored cigarettes; to put tobacco company logos on display at sporting, athletic or entertainment events or on clothing and other promotional items; and to place outdoor tobacco ads within 1,000 feet of schools and playgrounds. In addition, tobacco companies will be prohibited from using misleading terms such as “low tar,” “light,” or “mild” to describe their cigarettes. Cigarette packages will carry larger warning labels, up to 50% of the surface of one side. And depending on studies to be conducted by the FDA, tobacco companies may be required to reduce the amount of nicotine in cigarettes.

## Influenza and Asthma

### A Recurrent and Evolving Threat

Throughout the world, influenza virus pays an annual and unwelcome visit to people and other animals. It is one of the respiratory viruses, making its way into our bodies via the nose and throat and often spreading into the lower respiratory tract (our bronchial tubes and, sometimes even the substance of our lungs, the millions of tiny air sacs, called alveoli, causing pneumonia). Sometimes infection with influenza virus is indistinguishable from a common cold.

Sometimes it causes a more serious illness, characterized typically by high fevers, diffuse muscle aches (“like someone beat me up”), and overwhelming weakness and fatigue.

As we have all been reminded this year, not all strains of influenza are the same. The influenza virus can vary in the proteins that it puts on its surface, influencing how it infects our bodies and how our immune systems react to it. Usually the changes in the surface proteins vary little from one year to the next, so that the illness caused by these germs, commonly known as the “flu,” is similar year after year.

However, every once in a while, as this year, the coating proteins make an abrupt and dramatic change, combining elements from strains of influenza in people, pigs, and birds. And our immune systems are less well prepared to fight off what appears to them as a new and unfamiliar germ. This year’s new strain of influenza, for a time referred to as “swine flu” and now more properly referred to as an H1N1 strain of influenza A, has spread with incredible speed around the entire world. Like most respiratory viruses, influenza is readily spread from person to person. An infected person shares the germs by coughing and sneezing. We acquire the germ either by directly breathing it in or, more often, on our hands, which have touched infected secretions or surfaces and then have moved to touch our own face around nose and mouth. Because of the irresistible speed with which H1N1 influenza is spreading worldwide and the expectation that millions of people will be infected, the World Health Organization has declared the illness caused by this germ a “pandemic.”

People with asthma are probably no more likely that



*An influenza virus*

anyone else to get infected with influenza. But if you do suffer the flu, it may affect you more seriously. Like any of the respiratory viruses, the “flu” can cause a flare of your asthma. It can not only cause cough and chest discomfort by spreading to infect the bronchial tubes, but it can stimulate a full-blown asthmatic attack (as viral respiratory infections often do). Sometimes influenza can cause pneumonia, a very serious viral pneumonia involving both lungs. And if at your best you have compromised lung function, as occasionally people with asthma do, a viral bronchitis or pneumonia can be particularly devastating (as it is in those with advanced COPD or emphysema).

### How to Protect Yourself?

If you have asthma, what should you do to protect yourself? Here’s the advice of doctors at Partners Asthma Center:

- Get vaccinated against influenza this fall when the “flu vaccine” becomes available (usually starting in late September or October).
- If possible, avoid close contact with persons sick with respiratory infections (“head or chest cold”).
- Frequent hand washing helps, either with soap and water or with alcohol gels, like Purell.
- If you have had close contact with someone with definite influenza infection, contact your doctor. He or she may want to recommend anti-viral medication to prevent your becoming infected.
- If you develop a flu-like illness, with sore throat, nasal congestion, cough, high fever, and generalized muscle aching, contact your physician within 24 hours. The anti-viral medication, oseltamivir (Tamiflu), helps to kill influenza virus, shorten your illness, and make you feel better quicker.
- As always, be attentive to worsening of your asthma. Checking your breathing with a peak flow meter can help you judge how your asthma is doing. If you are having an asthma attack, it will need to be treated in the usual ways (with bronchodilators and corticosteroids) at the same time that you are treating the viral infection.

## Asthma Research at Partners Asthma Center

You may be interested in participating as a subject in a research experiment that leads to new information about asthma.

Partners Asthma Center is collaborating with researchers at the Asthma Research Center at Brigham and Women's Hospital in an important study of the treatment of asthma. This study asks about the influence that our genes may have in determining how we respond to different asthma medications.

There is evidence that depending on your genetic make-up, you may derive more or less benefit from regular use of the bronchodilator medications called long-acting beta agonists or LABAs. Formoterol (Foradil) and salmeterol (Serevent) are LABAs. They are part of the widely used combination inhalers (containing an anti-inflammatory steroid plus a LABA), called Advair and Symbicort.

The question being asked by this research study is whether an alternative long-acting bronchodilator—a medication that is not a LABA and that works by a different pathway altogether—might be better for you, depending on your genetic make-up. If you have asthma and take Advair or Symbicort, you may be eligible to participate in this study.

The experiment is called GABLE, for Genotype Stratified Treatment with Anticholinergic vs Beta-Agonists (Long Acting) and Exacerbations. In it, some patients will continue to use their LABA, others will be switched to an alternative long-acting bronchodilator, called tiotropium (Spiriva). Everyone in the study continues to take an inhaled steroid as part of their regular controller therapy. The genetic analysis is done via a routine blood test. The study lasts 52 weeks and involves 4 visits to the Asthma Research Center. Subjects are paid for their participation—in addition to the satisfaction of contributing to our understanding of asthma and its treatment.

If you would like more information about GABLE, please call 617-732-8201 (or 888-99ASTHMA).



### *Asthma and Reflux, from page 1*

the subjects in the study were tested for acid reflux; and half were given an intensive treatment to neutralize stomach acid (esomeprazole or Nexium taken twice daily), whereas the other half received an identical-looking placebo tablet to be taken twice daily. The outcome: 40% of the subjects had asymptomatic acid reflux, but treatment with a powerful therapy to treat their “silent reflux” had no impact on their asthma. Their asthma was not better controlled if they took esomeprazole rather than placebo. They did not feel better, they did not have better lung function (peak flow tests), and they did not experience fewer flare-ups of their asthma.

So, now we know. If you have asthma and troublesome symptoms of GERD, it is worthwhile treating the acid reflux. You will feel better, protect your esophagus from harmful effects of stomach acid, and perhaps help to get your asthma under control. But if you have asthma and are not troubled by symptoms of acid reflux, then it is *not* worthwhile taking treatments for acid reflux on the possibility that silent reflux is making your asthma worse. Asymptomatic reflux is not the cause of poorly controlled asthma; it is necessary to look elsewhere.

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