Stress and Asthma: Searching for the Link

It wasn’t that long ago that asthma was considered a disease of the mind, a psychosomatic illness referred to in medical texts as *asthma nervosa*. In effect, the “blame” for having asthma was placed on the asthma sufferer: if only you were psychologically more well-balanced, your breathing would be fine! And so too, according to some medical practitioners of the time, would your ulcers, your back pain, your headaches, and your colitis.

Modern science has made huge strides in understanding the biologic mechanisms of asthma, and more and more evidence indicates that the problem is in your breathing tubes, not in your head. We understand asthma to be a condition of the bronchial tubes, sensitized by an allergic type of inflammation, vulnerable to narrowing when stimulated by allergens, irritants, infections, or other triggers that provoke more swelling of the walls of the tubes and tightening of the muscles that surround the tubes.

Exploring the mind-body connection

Still, the mind-body connection is strong, and as a person with asthma you may identify stress as one of those triggers that can make your asthma worse. Your breathing was fine until... (fill in the blank)... you had a fight with your boyfriend, your boss criticized you for something that could not be avoided, the bills piled up beyond your ability to pay them, or your day in divorce court loomed. Many people have had the experience that strong negative feelings such as fear, anger, deep sadness, or anxiety, provoke their asthma symptoms of shortness of breath and tightness in the chest.

How might stress make your asthma worse?

One might dismiss stress as mimicking asthma symptoms. Even those who don’t have asthma can feel breathless and tight in the chest when heavily stressed, like that moment in childhood when you were asked to perform before a large audience for the first time! Or stress may compound the sensations of asthma: if you are wheezing and short of breath, stress will undoubtedly make you feel worse, whereas security and support will likely make your symptoms less intense. However, other explanations are possible: while sudden or brief stress may release in your body hormones that generally help your breathing (like cortisol and adrenaline), chronic stress may have negative effects on the healthy balance of these hormones. Our reaction to stress may also impact on our immune system and the nerve pathways through the body. And then there are the indirect ways in which stress can lead to worsened asthma control. For instance, it can make you more likely to smoke cigarettes, to overeat, to miss your doctor’s appointments, or find the energy to take good care of your health in general.

Physical violence as a potent form of stress

Recently, researchers in Boston and elsewhere have wondered whether stress might contribute to the disproportionate burden of asthma severity found among the urban poor. Living in poverty imposes huge stresses on a daily basis, but one example seems to stand out from the rest: the stress of experiencing or witnessing physical violence. The frequency with which violence intrudes into the lives of children in our... continued on p. 3
Proposed warning about omalizumab (Xolair)

In February the Food and Drug Administration (FDA) asked Genentech, the makers of the anti-IgE monoclonal antibody, omalizumab (Xolair), to add a warning to their patient information (“package insert”). The warning is meant to alert users of omalizumab about the potential risk of anaphylactic reactions to the drug.

Omalizumab is a biologically-engineered molecule designed to bind to the allergy protein, called immunoglobulin E (or IgE), as it circulates in the blood and to remove it from the circulation. The consequence is that much less IgE is available to attach to allergy cells (mast cells) and with allergens trigger the allergic reactions of asthma. For some patients with asthma that has been difficult to control with other asthma medications, omalizumab has proven helpful in controlling asthma and reducing the frequency of asthmatic attacks. Omalizumab (Xolair) is administered by injection every 2 or 4 weeks, depending on the dose required.

The FDA has accumulated information about the frequency of serious allergic reactions experienced by patients to whom the medication has been administered (since its release in 2003). They have found that one in one-thousand patients (0.1%) have suffered an anaphylactic reaction attributed to the medication. Anaphylaxis (pronounced anna-phil-LAX-iss) was defined as a serious allergic-type reaction characterized by wheezing and shortness of breath, light-headedness, generalized hives, and swelling in the throat. In its most serious form, anaphylaxis can cause very low blood pressure and loss of consciousness.

Most of these anaphylactic reactions have occurred after the first administration, and most have occurred within the first two hours after the injection was given. But the FDA recently warned that some anaphylactic reactions can occur after having safely received the medication for weeks or months and that some reactions can be delayed, occurring more than two hours after administration. No deaths were reported following injection of omalizumab.

As a result of this information accumulated since the initial release of omalizumab (“postmarketing data”) — and in accordance with the recommendations of the FDA — Partners Asthma Center has asked that all of our patients receiving omalizumab take the following precautions, even though your risk is very small: 1) wait under medical observation for two hours after you receive your omalizumab injection; and 2) for the 24 hours after your injection, carry with you a syringe pre-filled with epinephrine (EpiPen or Twinject). The treatment for anaphylaxis is immediate injection of epinephrine under the skin… followed promptly by urgent medical attention.

New medications

A new nasal steroids spray, fluticasone furoate (Allermist), has proven effective for the treatment of allergic rhinitis. FDA approval is being sought by its manufacturer, GlaxoSmithKline. Clinical trials among patients receiving this nasal steroid spray found — curiously — that many reported improvement in their allergic eye symptoms as well.

New asthma devices

The Flexhaler

The inhaled steroid, budesonide, used to treat asthma is currently available as...
inner cities is shocking: in a study conducted at Boston Medical Center, 10% of children witnessed a knifing or shooting before 6 years of age; 18% witnessed shoving, kicking, or punching, and 47% heard gunshots. Exposure to the extreme stressor of physical violence may somehow—by mechanisms not well understood—contribute to difficult-to-control asthma, just like exposure to dust, animal danders, and cigarette smoke. Some have described this pervasive stress of family and community violence as a “social pollutant” that enters the body through the mind rather than the airways.

Psychological stress is here to stay. But it may be that stress reduction is an important part of asthma therapy, at least for some people. Young children in particular deserve the chance to live a childhood where stress is minimized, particularly the extreme and psychologically lingering form of stress that is physical violence and abuse.

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**Breath of Fresh Air**

a liquid for nebulization (Pulmicort Respules) and as a dry-powder inhaler (Pulmicort Turbuhaler). The makers of budesonide (Astra Zeneca) are soon to release a new dry-powder device for their budesonide inhaled steroid, called the Flexhaler. It will have three features that distinguish it from the Turbuhaler (which will gradually be phased out). First, it will be available in two different doses, one similar to the current Pulmicort Turbuhaler, one at half the amount (180 mcg per puff and 90 mcg per puff). Second, it will have a built-in dose counter, indicating how many doses remain in the container. Third, it will have a slight taste (of lactose), making it easier to identify that the medication that you breathed in has actually been delivered.

**Flexhaler**

Available by prescription, MD Turbo is a device designed to optimize use of your metered-dose inhalers. Most metered-dose inhalers fit within this plastic, palm-sized device. MD Turbo offers two special features. First, it provides a dose counter (programmed to start at 200 or 120 puffs, depending on the metered-dose inhaler), so that you can keep track of the exact number of puffs still available in each canister. Currently, only Ventolin-HFA brand of albuterol comes with a built-in dose counter. Second, it prepares each dose of medication to be released only upon inhalation. If you are familiar with the quick-acting bronchodilator, pirbuterol (Maxair Autohaler), you will recognize this concept of a breath-actuated inhalation system. By having the device release the medication only in response to your breath in, you are ensured of the synchronized timing of medication release and breathing. The goal is improved delivery of medication deep into your lungs.
Q & A: How will I know if I have an anaphylactic reaction?

A full-blown anaphylactic reaction is quite dramatic: you may feel flushed, itchy, and break out with hives in many places; you may feel light-headed, dizzy as though you were about to pass out; and, especially if you have asthma, you may develop severe wheezing and chest tightness. Many people develop swelling in the back of the throat, at times so severe that it becomes hard to swallow and to breathe. You may experience a horrible overall sense of doom. Put another way, anaphylactic reactions can involve the skin, the bronchial tubes, and the throat; it can also cause the small blood vessels to dilate and leak fluid, leaving you with low blood pressure and the danger of passing out.

Anaphylaxis results from an allergic reaction that takes place in the bloodstream. As a result it usually develops in response to allergic stimuli that are either ingested (like certain foods or antibiotics) or injected (like bee stings or medication reactions). Unlike asthmatic attacks, it rarely develops in response to allergens that are inhaled.

The reaction can come on within minutes of an allergic exposure (for example, to intravenous contrast dye for an X-ray test) or may be delayed up to an hour afterwards and rarely longer.

Imagine that your child experiences light headedness and a lump in the throat after eating a peanut-butter cookie. He or she looks pale and complains of itching all over. What can you do? Here are three things to do, without delay. First, have him lie down, if possible. In the setting of low blood pressure, blood will have an easier time getting from his heart to his brain if he is not sitting or standing. Second, give him an injection of epinephrine. Use the EpiPen or Twinject that you or he always keep on hand. And third, call for emergency help, most readily by dialing 911.

About the pre-filled self-injecting syringe of epinephrine (EpiPen or Twinject), be sure to keep one close at hand and up-to-date (not expired). And don’t be afraid to use it. It may hurt for a moment (like any needle injection), but it may also save a life. Epinephrine will squeeze down on the blood vessels, helping to raise the blood pressure up toward normal; it will also treat an asthma attack and reduce swelling that occurs in the throat. In very large people (over 250 pounds), a larger dose (two injections) may be necessary.

The auto-injectors are designed to deliver medication through clothing, if necessary. The injection should be given in the middle of the thigh (halfway between groin and knee), on the top of the thigh or slightly laterally (toward the side away from the other leg).

How to use the EpiPen

Here’s how to use the epinephrine auto-injector (the following description pertains to the EpiPen brand). Screw off the top of the outer plastic holder and slide out the auto-injector device. Grab the auto-injector in the middle as you would wrap your hand around the handle of a bag or brief-case, with the thumb-side of your hand toward the gray top and the 5th finger (“pinky”) side of your hand toward the black cone tip, from which the needle will project. Pull off the gray protective plastic top (thumb-side); the device is now ready to use. With a quick, firm swing of your arm at the elbow, keeping your wrist steady, jab the black cone-tipped end of the device against the thigh and hold it there for 10 seconds. The needle automatically protrudes, and the medication is automatically delivered to just below the skin. Now pull out the injector and its exposed needle and gently rub the injection site along the thigh for 5–10 seconds. Dispose of the used needle by slipping it back into the plastic case and then bring it to a medical facility.

Once you have administered the epinephrine, proceed quickly to get emergency medical care.
New Members of Partners Asthma Center

Partners Asthma Center is pleased to have three asthma specialists join our ranks.

Aleena Banerji, M.D. is an allergist and member of Allergy Associates of Massachusetts General Hospital (Cox Building, MGH, Boston).

Anna Feldweg, M.D. is an allergist practicing in the Allergy Division at Brigham and Women's Hospital (850 Boylston Street, Chestnut Hill).

Rohit Ahuja, M.D. is a pulmonologist at Union Hospital in Lynn, part of the North Shore Medical Center.
Patient-Focused Spring Asthma Symposium

Tuesday, May 1, 2007
(World Asthma Day)

"Asthma Control: What to Expect and How to Achieve It"

6:00–8:00 p.m.
Duncan Reid Conference Room
Brigham and Women's Hospital
75 Francis Street

Come join us for presentations by Partners Asthma Center staff and informal discussion with questions and answers.