

Pamphlet #2: WHAT IS MEANT BY "INFLAMMATION" IN ASTHMA?

Central to our understanding of asthma and choices about its treatment is the concept of "inflammation" in asthma. Based on scientific discoveries over the last several decades, our view of what asthma is has changed dramatically. No longer is the focus exclusively on narrowing of the breathing passageways (bronchial tubes) due to contraction of the bronchial muscles that surround these tubes (referred to as "bronchospasm"). Increasingly, there is emphasis on the importance of inflammation of the bronchial tubes and treatment with medications that reduce this inflammation (anti-inflammatory drugs). This pamphlet discusses what is meant by inflammation in asthma, and why it is so important to treat this inflammation, even if it is not causing us any symptoms, such as cough or wheeze or shortness of breath.

Other Examples of Inflammation

Inflammation is a term used in medicine to describe how the body reacts to various types of injury, irritation, or infection. Inflammation takes various forms. A sunburn is a type of inflammation of the skin in reaction to the ultraviolet rays of sunshine. The rash of poison ivy is another kind of inflammation of the skin, an allergic reaction to oily resins on the leaves of the poison ivy plant.

Inflammation Can Be Acute or Chronic

Like these two examples, some types of inflammation last for only a brief while and then go away when the cause of the irritation is removed. However, other types of inflammation can last for months or years or even a lifetime. Still considering inflammation of the skin, psoriasis is an example of a long-lasting or chronic inflammation. Similarly, rheumatoid arthritis is a chronic inflammatory disease of the joints of the body.

Whether it is brief (acute) or long-lasting (chronic), inflammation can go away without leaving a trace. Other times, inflammation can leave behind scarring and permanent changes in the body.

During Attacks of Asthma, the Bronchial Tubes Become Acutely Inflamed

It has been known for a long time that acute inflammation of the bronchial tubes occurs during asthma attacks. The bronchial tubes become swollen and narrowed and mucus is secreted into the tubes from glands in the walls of the tubes. Swelling of the tubes and their plugging with

mucus make it difficult to breathe. You may cough up some of this thick, gooey mucus during a flare of your asthma.

Asthma Is a Chronic Inflammation of the Bronchial Tubes

An important medical discovery at the end of the last century was that some inflammation is present in the bronchial tubes of most persons with asthma even when feeling well and when breathing is normal. The cause of this chronic inflammation is not fully known, although in many instances it has the appearance of an allergic-type reaction. The inflammation may be mild, so mild that it does not cause narrowing of the bronchial tubes. But the persistent or chronic presence of the inflammation probably contributes to making the bronchial tubes capable of narrowing abnormally. The bronchial tubes in asthma are said to be "twitchy" or easily sent into spasm or narrowing. What makes the bronchial tubes "twitchy" or vulnerable to a variety of stimuli in the world around us -- whether it be dust or exercise or cat dander or cold air -- is at least in part the persistent presence of inflammation in the bronchial tubes.

Ways to Reduce Inflammation in Asthma

We do not yet know how to turn off fully the inflammation of asthma. There are, however, effective ways to reduce it. The first is to identify those things that are stimulating the inflammation in the first place and to rid them from the environment, meaning from the air that we breathe. Some things, like cigarette smoke and air pollution, are likely to worsen the inflammation of the bronchial tubes in anyone with asthma. Other things, like cat dander or house dust, cause asthmatic inflammation only in those persons who are specifically allergic to cats or dust mites. Sometimes allergy testing is useful to identify those things to which an individual is allergic, with the goal of reducing or eliminating the amount of exposure to them (see the pamphlet, Allergy Testing in Asthma, prepared by the Mass General Brigham Asthma Center). In a highly allergic person with asthma, allergen immunotherapy ("allergy shots") may have a role in blocking or blunting asthmatic reactions to specific allergens to which one continues to be exposed.

Medications Can Help to Reduce the Inflammation of the Bronchial Tubes

The other principal way to reduce the chronic inflammation of the bronchial tubes is to take medications that suppress it. These are the anti-inflammatory medications of asthma. By damping down asthmatic inflammation of the bronchial tubes, they improve breathing and, importantly, reduce the likelihood of acute asthmatic flare-ups or "attacks." They are designed to make the bronchial tubes look and behave more like normal, and so be less "twitchy."

The most widely recommended of these medications are the anti-inflammatory corticosteroids ("steroids") taken by inhalation. They are similar to the topical corticosteroids that you might apply to your skin for a chronic allergic skin rash like eczema. Sometimes they are taken alone

(brand names include *Alvesco*°, *Arnuity*°, *Asmanex*°, *Flovent*°, *Pulmicort*°, and *Qvar*°), and sometimes they are prescribed as a combination inhaler that also includes a bronchodilator to relax the bronchial muscles (brand names include *Advair*°, *AirDuo*°, *AirSupra*°, *Breo*°, *Dulera*°, *Symbicort*°, and *Wixela*°).

Another group of anti-inflammatory medications, taken as tablets, are referred to as "anti-leukotrienes" or "leukotriene modifiers" because they block one class of chemicals that promote inflammation in asthmatic bronchial tubes, the leukotrienes (pronounced: loo-ko-try-eens). Although helpful in some persons with asthma, they are not generally as effective as the inhaled steroids. Brand name leukotriene modifiers include *Accolade*°, *Singulair*°, and *Zyflo*°.

Most recently, a group of medications have been developed that very specifically block key molecules important in promoting asthmatic inflammation of the bronchial tubes. As a group, these highly targeted proteins, given by injection, are known as monoclonal antibodies and are often referred to as "biologics." More and more, monoclonal antibodies are being used to treat a variety of chronic inflammatory diseases, including inflammation of the joints (rheumatoid arthritis), skin (psoriasis and eczema), and colon (ulcerative colitis). In asthma they are currently reserved for hard-to-control disease that fails to improve with inhaled steroids and/or leukotriene modifiers. Examples include *Cinqair*, *Dupixent*, *Fasenra*, *Nucala*, *Tezspire*, and *Xolair*.

These medications can keep the inflammation of the bronchial tubes at a minimum while you take them; if you stop the anti-inflammatory medications, the inflammation of the bronchial tubes usually returns within a few weeks to what it was before taking the medications.

A novel approach to treating asthma involves administering an inhaled steroid together with a quick-acting bronchodilator whenever asthma symptoms call for rapid relief. This treatment approach, referred to as "anti-inflammatory reliever" or "AIR," has been shown to reduce the frequency of serious asthma attacks. It turns out that taking a medicine to reduce inflammation every time that you have active asthma symptoms seems to deliver just the right amount of inflammation-reducing medication at just the right time.

The "Non-Steroidal Anti-Inflammatory Drugs" Do Not Work for Asthmatic Inflammation

One type of anti-inflammatory medication works for the inflammation of arthritis but is not effective in asthma. These are called the "non-steroidal anti-inflammatory drugs" or NSAIDs. Examples include aspirin, ibuprofen, naproxen, Advil*, Motrin*, Naprosyn*, Ansaid*, ketorolac, and many others. Not only does this group of medications not help to treat the inflammation of asthma, but in some persons with asthma — those identified with "aspirin-exacerbated respiratory disease" — any of these NSAID medicines can bring on an attack of asthma, often one that is quite severe (see the pamphlet, Asthma and Aspirin Sensitivity, prepared by the Mass General Brigham Asthma Center).

Preventive Treatment in Asthma

When severe swelling of the bronchial tubes and excessive mucus production cause cough, wheezing, and shortness of breath, it is clear that powerful anti-inflammatory medications are necessary to restore comfortable breathing. But why is it recommended for many persons with asthma that they take their anti-inflammatory medications every day, even when feeling well? The idea is that by reducing the chronic, persistent inflammation that is present, the underlying sensitivity or "twitchiness" of the bronchial tubes lessens. One becomes less vulnerable to the possibility of developing an attack of asthma from severe swelling and bronchial muscle spasm. Anti-inflammatory medications are protective or preventive. They often need to be taken every day to prevent the symptoms of asthma from developing. In persons whose asthma has been active and troublesome, the goal of successful asthma care is to prevent the symptoms of asthma from developing rather than repeatedly having to relieve them with medications once they have occurred.

The Anti-Inflammatory Medications Are Safe to Use Every Day

The medications used to treat inflammation in asthma have been in use for more than 50 years. They are believed to be safe when used every day: they do not lose their effectiveness over time; they do not cause you to become dependent ("addicted") to them; and they rarely cause serious medical problems even after decades of use.

No cure yet exists for asthma, but regular use of anti-inflammatory medicines can make the inflamed bronchial tubes of asthma more like normal, the symptoms of asthma gradually to go away, and the risk of a serious asthma attack far less likely.