



Leukotrienes' Role In Asthma

Singulair and Accolate

Asthma is a chronic, or ongoing, disorder that is caused by inflammation of lung tissues and is marked by a tightening of the bronchial tubes, which causes wheezing and shortness of breath. In addition, the body produces more mucus than normal, which can clog the lungs.

Researchers now are beginning to understand the chain of events that occur at the cellular level during an asthma attack. An asthma trigger, such as cat hair or dust, starts a series of chemical reactions in the body that produces several substances, including a family of molecules known as leukotrienes.

Leukotrienes play a key role in asthma in three ways: causing inflammation, bronchoconstriction and mucus production. The cysteinyl leukotrienes (LTC 4 , LTD 4 and LTE 4) have been shown to be the most potent bronchoconstrictors in humans and are believed to play a crucial role in asthmatic airway obstruction. Leukotrienes may attract white blood cells to the lungs, increasing swelling of the lung lining. Leukotrienes also increase mucus production and make it easier for fluids to accumulate (an important part of inflammation).

Histamine is probably the mediator most well known. And for people with allergies, anti-histamines play a key role in alleviating symptoms. But for people with asthma, important mediators include prostaglandin D 2 , platelet activating factor, leukotrienes and other chemicals involved in inflammation. The mediators that may play the most critical role are leukotrienes. The leukotrienes are known by their initials: LTB 4 , LTC 4 , LTD 4 and LTE 4 .

Leukotrienes are involved in all three aspects of asthma's symptoms, LTD 4 , for example, is believed to be the most important cysteinyl leukotriene in the pathophysiology of asthma because of its potent bronchoconstrictive effect (at least 200 times stronger than histamine), causing the muscles around the airways to tighten. Additionally, leukotrienes have been shown to call white blood cells to lung tissue, potentially contributing to the swelling of the lung's lining.

Leukotrienes also make it easier for fluids to leak into tissues where they don't belong. This adds to inflammation and swelling, but also gives irritants in the fluids access to the tissues and muscles around the airway, contributing to the cycle of inflammation and bronchoconstriction. And, evidence suggests that leukotrienes increase mucus production.

What This Means For Treatment

The understanding that leukotrienes may lead to asthma symptoms is relatively new. If scientists could block some of the actions of leukotrienes, they could reduce inflammation, bronchoconstriction and mucus production. In short, stopping the action of these chemical mediators might stop the progression of asthma in some patients.

The first new class of the leukotriene modifiers blocks the effects of cysteinyl leukotrienes including LTD₄. The first drug in this class, called ACCOLATE[®] (zafirlukast) is available by prescription from Zeneca Pharmaceuticals.

The second available drug, SINGULAIR[®] (montelukast) is available as a once-a-day drug by Merck Pharmaceuticals. The drug works best when taken before bedtime.

Another class of drugs (often called 5-LO inhibitors) acts to block leukotriene synthesis. The first in this new class is available by prescription as Zyflo[®] (zileuton) from Abbott Laboratories.