

Pamphlet #10: ASTHMA AND ASPIRIN/NSAID SENSITIVITY

For the vast majority of persons with asthma, taking aspirin or a related non-steroidal anti-inflammatory drug (NSAID, pronounced as the letter “N” followed by the word “said”) has no effect on their asthma, neither good nor bad. However, for as many as 7% of persons with asthma, aspirin or any other NSAID, such as ibuprofen (*Advil*[®], *Motrin*[®]) and naproxen (*Aleve*[®], *Naprosyn*[®]), can cause asthma to worsen, often in the form of a severe and sudden attack. Besides causing symptoms of asthma, aspirin can cause nasal congestion and abdominal pains in susceptible individuals. Most often, this sensitivity to aspirin develops in adulthood. It often is found in conjunction with nasal polyps (growths of extra nasal tissue that plug the nasal passageways). Because frequently both lungs and nose/sinuses are involved, the condition has been termed more generally “aspirin-exacerbated respiratory disease” (AERD, pronounced as the 4 separate letters in 4 syllables).

What causes aspirin/NSAID sensitivity?

There is much that we don’t know about AERD, including most notably, what causes it. It is not an inherited trait passed on from one generation to the next; it is not genetic. Maybe it is triggered by a virus. We know that aspirin and other NSAIDs have biochemical actions that relate indirectly to the leukotrienes (pronounced loo-ko-**try**-eens), chemicals important in inflammation and bronchial muscle contraction in asthma. Persons with AERD tend to make excess amounts of leukotrienes. It is possible that an imbalance in the regulation of these biochemical pathways leads some people with asthma to be vulnerable to the effects of aspirin and other NSAIDs. This intolerance of aspirin and other NSAIDs is not strictly speaking an allergy. It is not more common in persons whose asthma is made worse by allergens such as animal danders, dust mites, mold, pollens, etc.; and it does not involve the cells (like mast cells) or antibodies (like immunoglobulin E, IgE) that are central to causing allergic asthma. Nor is it a specific medication “allergy” like penicillin allergy. If you have an asthmatic reaction to aspirin, you will experience the same reaction to all of the NSAIDs, and vice versa (so that if you experience an asthmatic reaction to ibuprofen, you need to avoid aspirin and all of the other NSAIDs).

AERD is rare in children. Adults most commonly develop this sensitivity to aspirin/NSAIDs in their 30s and 40s. It can occur in persons with long-standing asthma, or it may develop when asthma is just beginning. The development of their nasal polyps may occur around this same age. Many persons with asthma have been advised by their medical providers as a general

precaution to avoid aspirin, just in case you were at some point to develop an intolerance to aspirin. At the MGB Asthma Center we do not give this warning, since more than 90% of persons with asthma will tolerate these medications without any adverse reaction throughout their entire lives.

“How do I know if I have aspirin/NSAID sensitivity?”

Most persons find out that they have AERD by direct experience when they suffer an asthmatic reaction to aspirin or any NSAID. The reaction typically develops 30-90 minutes after ingestion of the medication. It is not the non-specific stomach upset that many people have had after taking this family of medications. It is a striking worsening of asthma and often severe nasal congestion and drip. For those who are uncertain as to whether they might have experienced such a reaction and need to take one of this family of medications (for example, aspirin for prevention of heart attack or stroke or other NSAIDs for arthritis), it is possible to be tested for aspirin/NSAID sensitivity in a safe medical setting. Many allergists offer an “aspirin challenge” in their medical office, beginning with a fraction of a tablet of a “baby aspirin” (81 mg) and gradually increasing the dose while observing for any adverse reaction. The AERD Center at Brigham and Women’s Hospital (<https://www.brighamandwomens.org/medicine/allergy-clinical-immunology/allergy-aerd-center>) has performed hundreds of such aspirin challenges.

Treatment

The treatment of asthma and of nasal polyps in persons with aspirin/NSAID sensitivity is fundamentally the same as in persons without this unique characteristic. Bronchodilators and inhaled corticosteroids remain the cornerstones of treatment for their asthma and are just as effective in persons with aspirin/NSAID sensitivity as they are in those without it.

The best protection is avoidance.

Most important is avoidance of all aspirin/NSAIDs, including all combination products that may include these medications. NSAIDs make up a long list of medications besides ibuprofen and naproxen, including both over-the-counter and prescription drugs. A few examples include diclofenac (*Voltaren*®), indomethacin (*Indocin*®), ketorolac (*Toradol*®), meloxicam (*Mobic*®), nabumetone (*Relafen*®), and tolmetin (*Tolectin*®). Aspirin is sold under a variety of brand names, including *Ascriptin*®, *Aspergum*®, *Bufferin*®, *Ecotrin*®, and *Halfprin*®. Even the smallest amount of aspirin (for example, an 81 mg/tablet) can cause a severe reaction and should be strictly avoided.

In addition, many over-the-counter remedies for headache, cold symptoms, fever, body pains, and more contain aspirin or other NSAID, such as *Alka-Seltzer Original*®, *Anacin*®, *CVS Health Cold & Sinus Relief*®, *Excedrin*®, and *Vanquish*®. Persons with AERD need to be careful “bottle readers,” checking all of the ingredients of over-the-counter medications. If you are in doubt

about whether a medication is or contains aspirin or other NSAID, don't guess. Be certain by asking your pharmacist or other knowledgeable medical provider.

On the other hand, almost all persons with AERD can safely take acetaminophen (*Tylenol*®) without any fear of an adverse reaction.

Leukotriene-modifying medications

Because one finds increased amounts of the chemicals called leukotrienes in persons with AERD, it is logical to try anti-leukotrienes to treat this condition. There are two types of anti-leukotrienes. One type blocks the action of the leukotrienes after they have been formed. One widely prescribed example of this type is montelukast (*Singulair*®), a tablet taken once daily. Very similar is the twice-daily tablet, zafirlukast (*Accolate*®). The other type acts to block formation of the leukotriene chemicals in the first place. The one example of this category is zileuton (*Zyflo*®), a twice-daily tablet. Montelukast can rarely cause depression; zileuton carries a small risk of causing liver inflammation. Although sometimes quite helpful, none of the leukotriene-modifying medications is reliably effective in AERD; and none allows a person with AERD to safely take aspirin or other NSAID. Strict avoidance remains mandatory.

Biologics

More recently, the injectable medications used to treat severe, difficult-to-control asthma, referred to generally as “biologics,” have proved helpful in many persons with AERD whose asthma and/or nasal polyps have been refractory to conventional therapies. In particular, the monoclonal antibody therapy called dupilumab (*Dupixent*®) administered as an injection every 2 weeks has been enormously helpful for some patients. Other biologics are also approved for the treatment of refractory asthma and/or nasal polyps, including omalizumab (*Xolair*®), an injection given every 2 or 4 weeks depending on the dose needed, and mepolizumab (*Nucala*®), an injection given every 4 weeks. For more information about the “biologics” used to treat asthma, see the [pamphlet, Use of “Biologics” to Treat Severe Asthma \(in preparation\)](#), by the Mass General Brigham Asthma Center. Like the leukotriene modifiers, taking biologics for AERD does not allow safe ingestion of aspirin/NSAID medications.

Aspirin desensitization and maintenance therapy

It is, however, possible to be desensitized to aspirin, somewhat akin to a person who has had an allergic reaction to a bee sting can get desensitized to bee venom by receiving carefully graded, increasing amounts of injected bee venom until no longer allergic. In a carefully monitored setting (such as at the AERD Center at Brigham and Women's Hospital), a person with aspirin sensitivity can be given at first minute amounts of aspirin to swallow and then, in small, incremental doses, larger and larger amounts until over the course of several hours he or she can safely take a full-sized tablet of aspirin (325 mg) without any adverse reaction. Mild reactions are common and can be treated; severe reactions are rare but can also be managed

by the expert providers present during the desensitization procedure. NOTE: it would be dangerous and unwise to attempt desensitization at home!

Unlike the example of bee venom desensitization, for tolerance of aspirin to be maintained one needs to take an aspirin daily. If aspirin is omitted for 1-2 weeks, one's sensitivity to aspirin recurs, just as it was before desensitization. If desensitized to aspirin, one can safely take other NSAIDS with insignificant risk of reaction.

A curious observation was made among persons with AERD who were desensitized to aspirin and continued daily ingestion of aspirin: their nasal polyps and often also their asthma improved, sometimes dramatically. The usual recommended dose for treatment of AERD with aspirin following desensitization is 650 mg/day, although it is likely that for many persons this dose can be decreased somewhat over time. Potential side effects include, predictably, stomach irritation and bleeding. Exactly how this therapeutic approach, referred to as aspirin desensitization and maintenance therapy or ADAM, works to improve AERD remains as much of a mystery as what causes AERD in the first place.