

# The AERD Center

at Brigham and Women's Hospital

Information for patients with aspirin-exacerbated respiratory disease (AERD) / Samter's Triad

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## MESSAGE FROM OUR DIRECTORS

We enrolled our 241<sup>st</sup> patient into the AERD Registry in April. Without your generous donation of time it would not have been possible – Thank you. We continue to recruit new patients to allow us to carry out meaningful studies with our data, and assess trends from analyses of your cells and clinical information. We have started presenting preliminary findings from these studies at Allergy/Immunology and Asthma conferences around the world. You can read more about our findings and what we presented on *page 3* and at <https://aerd.partners.org>. We thank you for dedicating your time to research that will hopefully begin to answer some of the many remaining questions about AERD.

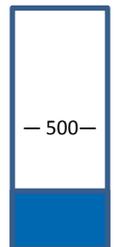
- Drs. Tanya Laidlaw, Katherine Cahill, & Joshua Boyce

## BY THE NUMBERS

Enrollment has been going very well for participation in the AERD Registry, and we are now able to mail out a Consent Form and enroll patients through the mail, even if they have never been seen as a patient here. We have recruited 241 patients, with a goal of bringing 1,000 AERD patients into the Registry. A look at the Registry to date shows:

- 55% of the patients in the AERD Registry are female
- Average age is 48 years old
- The average age at which participants developed nasal polyps for the first time is 38 years (range = 12-65 years)
- Most of the patients experience decreased sense of smell (hyposmia) or total lack of smell (anosmia)

GOAL: 1000



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## MEPOLIZUMAB (NUCALA®)

Nucala® is a new medication recently approved by the FDA. It is indicated for add-on maintenance treatment of patients with severe asthma, aged 12 years and older, who have an eosinophilic type of asthma. Nucala® is given by subcutaneous injection every 4 weeks.

The active component of Nucala® is an antibody that works by reducing the effect of IL-5, a mediator involved in the growth, differentiation, recruitment, activation, and survival of eosinophils, a type of immune cell that are often abundant in patients with AERD.

In clinical trials, Nucala® was shown to significantly reduce the number of asthma exacerbations per year, and to reduce the need for oral corticosteroids in the patients studied. Please talk to your allergist if you would like more information.

## CORONARY VASOSPASM AS A CAUSE OF CHEST PAIN

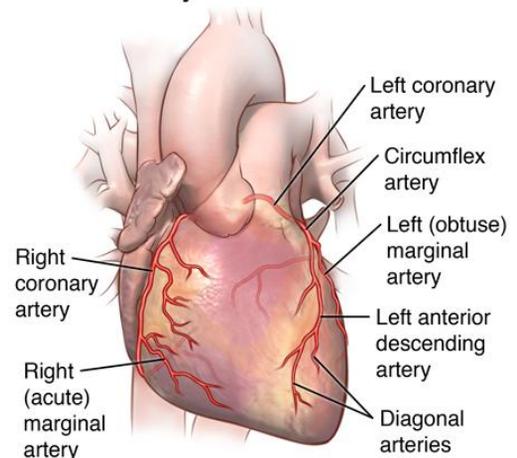
Our group at Brigham and Women's Hospital recently published a paper describing an unusual type of chest pain that some patients with AERD have experienced. Clinical observation and data support the cause of this chest pain may be due to coronary artery vasospasm. Coronary artery vasospasm occurs when the blood vessels that supply blood to the heart contract and restrict blood flow. This restriction of blood flow may be caused by the presence of eosinophils in the heart tissue.

After reviewing 152 patient charts from our AERD Registry, it was found that 10 patients had experienced chest pain concerning for coronary vasospasm. Of the ten patients who reported chest pain, eight of them had been desensitized to aspirin. The pain worsened or first developed while on high-dose aspirin for six of those patients; for the

other two patients, chest pain started prior to aspirin and did not worsen on daily aspirin therapy.

It is too soon to know if use of high-dose aspirin therapy increases your risk for developing this type of chest pain. Continued involvement in our AERD Patient Registry will allow us to monitor for more cases and to investigate the cause of these symptoms. Eosinophil-suppressing treatments such as oral or IV corticosteroids have been effective in eliminating the chest pain and may even be lifesaving. *Seek medical help immediately if you experience chest pain.*

Coronary arteries of the heart



## HOW MUCH CAN WE LEARN FROM A MOUSE?

Over the past century, the laboratory mouse has become a quintessential tool in the study of human diseases, aiding in the discovery of novel treatments for cancer, diabetes, Alzheimer's, cardiovascular disease and now, AERD. As different as mice and humans appear, we share between 95-98% of our genome and have strikingly similar immune systems. Through genetic manipulation, we have created mice that develop AERD-like symptoms in response to aspirin.

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Using this mouse model, our group has begun to piece together the biological puzzle of AERD, hoping to determine the molecular and cellular interactions that cause the symptoms experienced by patients. In a paper recently published by our group, we identified a novel pathway in the activation of mast cells, one of the immune cells that produce large quantities of pro-inflammatory molecules. In the nasal polyps of AERD patients and in the lungs of aspirin-sensitive mice, we observed increased levels of a molecule called interleukin-33 (IL-33), a known activator of mast cells. When we inhibited IL-33 or its receptor in the mice, the severe inflammation and mast cell activation in the airways of the mice was significantly decreased, suggesting that IL-33 blockade could lessen the severity of AERD-like symptoms. This discovery is only one of many made possible by our AERD mouse model, providing us with molecular candidates for potential AERD therapeutics in humans.

## DEXPRAMIPEXOLE

Dexpramipexole is a medication that is currently being tested in a clinical trial for the treatment of chronic sinusitis with nasal polyps and eosinophilia. The study medication is a pill that is taken twice per day over the course of six months. The drug is believed to reduce eosinophils, a type of white blood cell that may contribute to the growth of nasal polyps.

We are now finished recruiting for this trial at Brigham in Women's Hospital in Boston, MA. Other participating sites are Boca Raton, FL; Baltimore, MD; Raleigh, NC; and Philadelphia, PA.

## CHANGING YOUR DIET

Patients with AERD have been shown to have elevated levels of inflammatory molecules called

leukotrienes. At Brigham and Women's Hospital, we are finishing up a clinical trial to see if it is possible to decrease levels of leukotrienes through dietary modification.

The diet we are investigating increases omega-3 intake, primarily through fish or fish oil supplementation, and decreases omega-6 consumption. Omega-6 is a fatty acid that the body can turn into inflammatory leukotrienes. We are monitoring patients for any improvement in their AERD symptoms after altering the omega-3/6 ratio.

Participants will come in for three visits over the course of one month and work closely with one of the study doctors and a nutritionist.



## ASPIRIN DESENSITIZATION STUDIES

While doses as small as half of a baby aspirin can trigger an allergic reaction in patients with AERD, daily treatment with high-dose aspirin (650 mg twice a day) is one of the few effective therapies that improves upper and lower respiratory function for many of these patients. In order for patients with AERD to start high-dose aspirin, an aspirin desensitization is required. It is unknown how the process of desensitization is achieved and how high-dose aspirin provides benefit. In order to understand the mechanism of aspirin desensitization and high-dose aspirin therapy, and to explore whether platelets are important in the disease, the Therapeutic Control of Aspirin-Exacerbated Respiratory Disease is being conducted at BWH. This research study uses a medication that

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is approved by the FDA, but not to treat asthma or AERD. The medication, prasugrel (Effient®), is an inhibitor of platelets, which we believe play a role in AERD. The purpose of this study is to find out if taking prasugrel will help treat the symptoms of AERD and prevent reactions to aspirin, and to learn why aspirin desensitization improves the respiratory symptoms of patients with AERD.

## AAAAI Update

The American Academy of Allergy, Asthma and Immunology (AAAAI) holds its annual conference bringing together clinicians and researchers from around the world to discuss new findings and promising treatments each year in early spring. Members of our team along with colleagues from Northwestern University in Chicago, IL, the Scripps Clinic in San Diego, CA, and the Karolinska Institute in Solna, Sweden educated physicians about when to consider the diagnosis of AERD and how to perform outpatient aspirin desensitizations. This year, Dr. Elena Jerschow from Albert Einstein College of Medicine reported on factors that predicted poor response to high-dose aspirin therapy in minorities, the first study to our knowledge looking at the effect of race on benefit to medical therapy among patients with AERD. Multiple investigators reported on the benefit of the monoclonal antibody omalizumab (Xolair®) which is approved for moderate to severe persistent allergic asthma, in patients with AERD. Promising new diagnostic tools for AERD were presented which may one day allow physicians to confirm a diagnosis of AERD without having patients undergo an oral aspirin challenge in the clinic. The meeting confirmed growing knowledge and interest in diagnosing, treating, and studying AERD, all of which are necessary to improve the care we can

provide to patients with AERD. It also motivated researchers and clinicians to push forward new ideas until we meet again in March 2017 in Atlanta, GA for a full program dedicated to sharing the latest in AERD research.



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