Summer 2023 Newsletter

The AERD Center

at Brigham and Women's Hospital

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

What's Inside

Message from our Directors

Over the last two years we have grown the AERD Center and expanded the research we are able to pursue – we now have three clinical research coordinators, a laboratory technician, a postdoctoral research fellow, a clinical research fellow, and a statistician. Luckily, we've been able to get some additional funding to support all the work we do, so we are excited to be able to say that – at least for now – we are full-steam ahead!

Our research this past year has concentrated on really trying to understand the mechanism of how/why each of the treatment options for AERD works. We've also focused on understanding the mechanism of why many AERD patients develop troubling reactions whenever they drink alcohol, and on finding out why patients' nasal polyps often grown back so quickly after sinus surgery. We continue to have several ongoing projects, and more starting up soon. Feel free to reach out to us by email with any questions to aerd@partners.org.

Dr. Tanya Laidlaw,
Dr. Kathleen Buchheit
& Jillian Bensko, PA-C

AERD Awareness Day
September 26th, 2023
Show your support by spreading awareness and learning more at www.samterssociety.org!

AERD Registry

Enrollment in our AERD Registry continues to grow, and our knowledge about AERD grows along with it. Be on the lookout for a new set of surveys that the AERD Center will be sending out by email in the next month (including questions about aspirin desensitization, treatment choices, and options for pain control) – we would greatly appreciate your participation!

BRIGHAM AND WOMEN'S HOSPITAL
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Publication: Immune Mechanisms in AERD

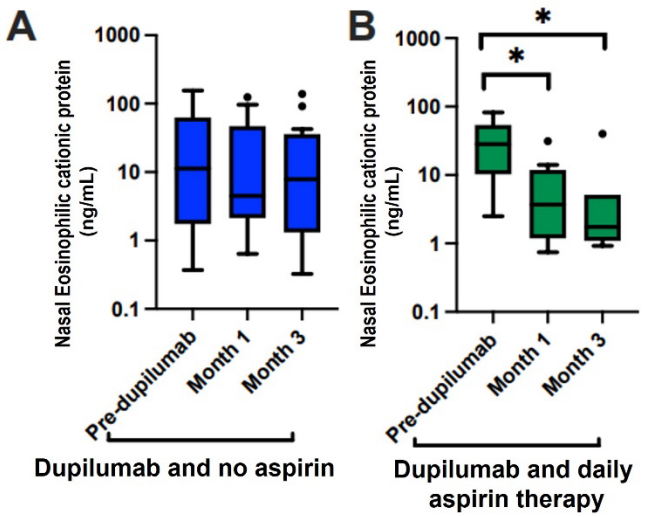
This review covers novel insights into the pathways of the immune system that may be affected in patients with AERD. Although we've known for decades that the mediators called "leukotrienes" are important causes of inflammation in AERD, their cellular sources and targets, and the contributions from other cells and mediators in AERD were unknown until recently. (PMID: 36184313)

Publication: Inhibition of Type 2 Inflammation with Dupilumab for Nasal Polyps

The pathway through IL-4Rα is usually considered to be a "Type 2 inflammatory pathway" and may be a cause of a lot of the inflammation in AERD. Given the widespread expression of IL-4Rα across many inflammatory cells in the lungs, nose, and sinuses, and the potential consequences that inhibition of IL-4Rα with the medication dupilumab may have, our goal with this study, led by Dr. Stella Lee, was to understand how the local inflammatory milieu of patients with nasal polyps changes after treatment with dupilumab. We observed a dupilumab-induced increased level of the cytokines IL-4 and IL-18 in the nasal secretions, as well as a trend toward increased CXCL8/IL-8. These may suggest a shift toward Th17/type 3 immune response, which may be indicative of a type 1/type 3 "escape" that occurs with inhibition of IL-4Rα. It has not yet been fully investigated how the local inflammatory environment changes in nasal polyp patients treated with dupilumab and there is more work to be done! Although exploratory—and thus limited in the conclusions we should draw from them —these preliminary data reinforce the need for further exploration of the consequences of inhibiting the type 2 inflammatory pathway. (PMID: 35394682)

Publication: Co-treatment with Daily Aspirin Therapy and Dupilumab Reduces Nasal Eosinophil Markers

Dupilumab and daily aspirin therapy are both used to treat asthma and nasal polyps in patients with AERD. However, we have not previously known if there is a benefit to using the two therapies together. In this study we assessed for clinical and mechanistic outcomes for AERD patients who were on daily aspirin therapy and dupilumab together versus dupilumab treatment alone. We found that patients who were on both daily aspirin therapy and dupilumab together had a reduction in nasal eosinophil markers (an inflammatory white blood cell that is often elevated in patients with AERD), whereas patients on dupilumab alone did not *[See figure below for the data]*. Our study supports the possibility that daily aspirin therapy and dupilumab work synergistically together to reduce respiratory inflammation in patients with AERD. It highlights the need for further studies to explore the clinical efficacy and mechanistic outcomes of daily aspirin therapy and dupilumab together (PMID: 37246613).

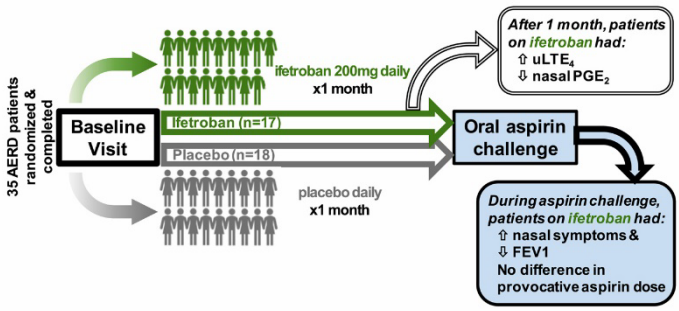


Summer 2023 Newsletter

The AERD Center at Brigham and Women's Hospital

Publication: Treatment with Ifetroban for AERD Patients

This clinical trial compared one month of treatment with ifetroban (a medication that blocks the thromboxane A2 receptor) to placebo in patients with AERD, to see if the ifetroban treatment decreased the severity of aspirin-induced reactions *[See figure below for the trial design]*. Unfortunately, there was a small signal showing that actually the treatment with ifetroban worsened some patients' reactions to aspirin. This was unexpected, and to further understand why, additional studies were done, where we found that ifetroban inhibited the production of prostaglandin E2 (generally a "good" player in AERD) and increased the levels of cysteinyl leukotrienes (generally "bad" players in AERD), which likely explains why our patients had a negative response to it. (PMID: 37068712)



Abbreviations: TP, Thromboxane receptor; AERD, Aspirin-exacerbated respiratory disease; $uLTE_4$, Urinary Leukotriene E_4; PGE_2, Prostaglandin E_2

Publication: Aspirin/NSAID Allergy and Postpartum Opioids

In this retrospective study, presence of an aspirin/NSAID allergy was associated with using more inpatient opioids immediately after childbirth. NSAID allergy was also associated with higher rates of opioid prescribing at hospital discharge following delivery. Multidisciplinary care involving obstetricians and allergy specialists prior to delivery may provide an opportunity for better planning to allow for the safest pain management and care, and to potentially decrease unnecessary postpartum opioid use. (Publication pending)

Current Research

Ongoing Study 1: Mechanisms of benefit of IL4Rα inhibition in AERD ("MARINER" study)

The aim of this study is to determine how the biologic medication dupilumab (anti-IL-4α) decreases nasal polyps and improves sense of smell in patients with nasal polyps and AERD. Using a prospective, open-label observational study design, approximately 30 adults with nasal polyps and AERD who meet criteria for the FDA-approved use of dupilumab for treatment of their severe nasal polyps will be followed to better understand how 8 weeks of dupilumab treatment affects clinical measures of disease severity in AERD, including nasal polyp burden, sense of smell, nasal congestion, respiratory-related quality of life, lung function, and asthma control. Clinical data and samples from both local (nasal fluid and nasal polyp biopsy) and systemic (blood and urine) sites will be collected at baseline, 2 weeks, and after 8 weeks of treatment with dupilumab and will be analyzed for a set of mechanistic assays to determine which cellular changes correlate with clinical benefit.

Ongoing Study 2: Assessing Long-Term Outcomes of Dupixent Treatment in Patients With Chronic Rhinosinusitis With Nasal Polyposis (AROMA)

AROMA is an observational study that is investigating the long-term effectiveness and safety of treatment with Dupixent® in adults with a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP). Participants will be asked to complete a series of questionnaires and diary entries to assess symptoms, how the symptoms change over time, and about overall satisfaction with treatment. AROMA does not require any additional clinic visits outside of your standard office visits and participants will be compensated for their time involved in completing the questionnaires. If you are 18 years or older and have recently been prescribed Dupixent ® to treat your nasal polyps, you may be eligible for participation.

The
AERD Center
at Brigham and Women's Hospital
Summer 2023 Newsletter
Page 4

Current Research

Ongoing Study 3: Mechanisms of alcohol induced reactions in AERD

In 2014, we completed a survey study that showed that the majority of patients with AERD experience alcohol-induced reactions, and that these reactions to alcohol are more severe than for patients who are aspirin tolerant. We are no pursuing research to fully understand why alcohol causes respiratory reactions in AERD.

Ongoing Study 4: 2-Year Follow Up of AERD Registry (2-FAR)

2-FAR is a 24-month long study examining the symptoms and disease progression for patients with AERD. We reached our goal of having 100 participants from the AERD Registry enrolled in this study and completed the final set of surveys in the fall of 2022. We measured how different treatments utilized for patients with AERD can impact health-related quality-of-life. A publication detailing the findings of the study is under review.

Ongoing Study 5: Biomarkers of Nasal Polyp Recurrence

We are working to identify biomarkers associated with nasal polyp recurrence after endoscopic sinus surgery in AERD. Nasal polyps can rapidly recur after sinus surgery in some patients with AERD, even when paired with aspirin therapy after desensitization. Using nasal polyp tissue and nasal mucus samples from patients who underwent endoscopic sinus surgery, we have planned proteomic, lipidomic, and cellular analyses of these samples to identify factors that predict nasal polyp recurrence. We hope to shed light on the causes of severe nasal polyposis and AERD and to identify novel therapeutic targets for this disease.

Where Are They Now?

After a wonderful two years as a Clinical research coordinator, Alanna McGill is currently a PA/MPH student at George Washington School of Medicine and Health Sciences.

Tessa Ryan spent two great years as a clinical research coordinator in the Laidlaw Lab, and is now a medical student at Tufts University School of Medicine.

New Staff

Laura Bailey, BA
Laura graduated from Hamilton College in May 2023, where she majored in Neuroscience. She now works as a clinical research coordinator in the Laidlaw Lab and is planning to go to medical school in the future.

Alyson Brown, BA
Alyson graduated from Wellesley College in May 2023, where she majored in Neuroscience. She now works as a clinical research coordinator in the Laidlaw Lab and is planning to go to medical school in the future.

Rose Corcoran, BA
Rose graduated from Hamilton College in May 2023, where she majored in Biology. She now works as a clinical research coordinator in the Laidlaw Lab and is planning to go to medical school in the future.

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