**Message from our Directors**

This year has been a very busy one, as we try to return to a sense of normalcy and care for our patients as safely as we can. We are continuing to push ahead with new research and new discoveries in AERD with the goal of providing the best possible treatments for our patients.

There are several new medications that have become available for the treatment of AERD over the past few years. In addition to offering them to our patients when appropriate, our research team has also been working hard to make sure that we fully understand how each of these medications works, and with those discoveries, we are starting to better understand what leads to the inflammation that causes AERD.

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

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**By the Numbers**

We are continuing to grow our AERD Registry and now have over 2,600 patients enrolled in our registry! As the data in our registry grows, so does our knowledge about AERD.

For example, data from our AERD registry participants showed us that on a scale of 0-5, 22.8% of them ranked their decreased sense of taste/smell as a 4 (severe problem) and 45.5% of patients ranked it as a 5 (problem as bad as it can be). This taught us that as researchers and healthcare providers, we need to pay more attention to the effects of anosmia, or loss of smell, and it inspired us to launch a new study about the potential impacts of smell loss. You can read more about what we learned about the impacts of anosmia on page 2 of the newsletter!

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**Ongoing Research**

- GLIDER study to investigate the global impact of dupilumab
- Updates on our longitudinal study 2-FAR
- Investigating if a new medication can block aspirin-induced reactions – Ifetroban trial
- Learning more about what IL-5 does in the immune system

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**New Staff**

Introducing our newest team members

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**AERD Awareness Day**

September 26th, 2022

Show your support by spreading awareness and learning more at [www.samterssociety.org](http://www.samterssociety.org)!
**Publication: Dupilumab-Associated Arthralgia in AERD Patients**

The advent of respiratory biologics for the treatment of CRSwNP and severe asthma for patients with AERD has led to significant improvements in patient quality of life, but post-marketing surveillance has revealed additional possible side effects. In April 2022, we reported a series of eight patients with AERD who developed arthralgias (joint pain) after initiating dupilumab. At the time of the study, we found 8 AERD patients out of the 160 (5%) who had been prescribed dupilumab at our center developed possible dupilumab-associated arthralgias. Several of the patients underwent extensive rheumatologic work-up, and no cause of the joint symptoms was found. All 8 patients experienced significant improvement in upper and lower respiratory symptoms after starting dupilumab and ultimately decided to continue dupilumab despite the arthralgias. Out of the 8 patients, the joint pain spontaneously resolved in 5 of them. The cause of this dupilumab-associated joint pain is still unknown and we have launched a new research study to learn more (see the GLIDER study on Page 4). We recommend that clinicians caring for patients who encounter this side effect consider close monitoring and continued treatment if the patient is otherwise benefiting from dupilumab. **PMID: 35124224**

**Publication: Pediatric-Onset AERD**

AERD is generally recognized as an adult-onset disease, however; the prevalence of AERD in pediatric patients is not well defined. In May 2022 we described a series of 6 pediatric patients with AERD, and their childhood AERD symptoms were almost identical to those in adults with AERD. In our AERD registry we found that more than 6% of the patients report that their AERD symptoms started before 18 years of age and noted that females tend to develop AERD earlier than males, and that developing AERD as a child is more common for girls than for boys. Additionally, all 6 adolescent patients in this series had severe enough disease symptoms that they were prescribed dupilumab as a treatment option, and all of them had good responses to dupilumab with improvements in both asthma and sinus symptoms. Therefore, we recommend that for adolescents with poorly controlled symptoms of AERD the potential benefit of treatment with dupilumab should be considered. **PMID: 35643277**

**Publication: Anosmia in AERD**

A common problem for AERD patients is loss of sense of smell, or anosmia, but its impact on patients’ quality of life, mental health, and physical wellbeing has been poorly studied. We developed a new questionnaire about the consequences of anosmia, which, along with several other quality-of-life questionnaires was sent to all our Registry patients. Eighty-five percent of the 853 patients who answered the questionnaires (Thank you!) reported diminished sense of smell and/or taste, and we learned that their loss of smell severely impacts their physical, emotional, and mental health. Many patients with diminished smell responded that they could not identify spoiled food (86%), did not enjoy food (71%), felt unsafe (63%), and had encountered dangerous situations (51%) because of their poor smell (see Figure below).

We think that the importance of sense of smell and the relevance of anosmia to patients’ lives should be acknowledged and evaluated by clinicians caring for these patients. **PMID: 35506180**
**Publication: How does Dupilumab work in AERD?**

Dupilumab, a “biologic” medication, is an antibody that inhibits the interleukin 4 receptor alpha and is effective for treating both nasal polyps and asthma in most patients with AERD, but the mechanisms by which treatment with dupilumab lead to clinical improvement are not completely understood. We analyzed the clinical and laboratory/mechanistic impact of treatment with dupilumab in 22 adult patients with AERD. After just one month of treatment with dupilumab, participants with AERD had remarkable improvement in their upper and lower airway symptoms, asthma control, sense of smell, and lung function, and these improvements were sustained after three months of treatment.

In terms of the mechanism of dupilumab, we found that treatment with dupilumab led to an increase in nasal prostaglandin E2 levels (an anti-inflammatory prostaglandin), and a decrease in nasal and urinary leukotriene E4 levels (an inflammatory asthma mediator). Nasal fluid prostaglandin E2 levels of participants who could not smell at the start of the study were significantly lower than those levels in patients who had a normal sense of smell, and the levels of prostaglandin E2 in the nasal fluid correlated with how many scents each participant could smell correctly. We suspect that prostaglandin E2 levels may be an important clue into loss of smell, and into why dupilumab works so well in AERD. We also found that dupilumab treatment reduced levels of IgE in the blood and nasal fluid and improved the function of the epithelial barrier in the sinuses.

This study, published in August 2022, provides important insight into the mechanisms of how dupilumab works in AERD and we think that dupilumab has effects on many cell types in the lungs and sinuses. **PMID: 35460728**

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**Publication: How does Mepolizumab work in AERD?**

Drugs targeting interleukin (IL) 5, such as the “biologic” medication mepolizumab, had been thought to work by targeting and decreasing eosinophils. Mepolizumab and other drugs that inhibit IL-5 can provide therapeutic benefit for patients with AERD, but we did not think that this was due only to their ability to decrease eosinophils.

We completed a case-control study of 18 patients with AERD who were on mepolizumab compared to 18 patients with AERD not on mepolizumab. In our study published in August 2021, we found that IL-5 inhibition with mepolizumab in patients with AERD decreases production of inflammatory eicosanoids like leukotriene E4 and increases levels of genes in the epithelial barrier of the sinuses that are needed to create a tight barrier. We suspect that mepolizumab, and other drugs that inhibit IL-5, work by decreasing the IL-5 signaling on mast cells and epithelial cells in the respiratory tissue, in addition to decreasing eosinophil numbers. **PMID: 34144111**
**CURRENT RESEARCH**

**ONGOING STUDY 1: Global immune effect of dupilumab on arthralgia**

GLIDER is a new study examining how blockade of IL-4Ra with dupilumab affects AERD patients’ immune systems. In particular, we want to understand why some patients develop joint pain as a side effect of dupilumab, while most others do not. We are evaluating changes in specific cells and inflammatory pathways of the immune system in patients who do or do not develop joint pain while on dupilumab. If you have AERD and take dupilumab and have developed new knee or other joint pain, please let us know. We are interested in finding out more about why this happens.

**ONGOING STUDY 2: 2-Year follow up of AERD Registry ("2-FAR")**

2-FAR is a 24-month long study that examines the symptoms and progression of disease in patients with AERD. We reached our goal of having 100 participants from the AERD Registry enrolled in this study and will complete the final 24-month set of surveys in the fall of 2022.

**ONGOING STUDY 3: Analyzing Ifetroban**

We have completed the enrollment for our trial of ifetroban, where we investigated whether taking the drug ifetroban, which blocks a receptor called the TP receptor, can block aspirin-induced reactions and may help treat AERD. We are still looking through all of our data for analysis and hope to have it finished for a publication by the end of 2022. Many thanks to all who participated!

**NEW STAFF**

**Laura Cho, BA**

Laura graduated from Wellesley College in May 2022, where she majored in Chemistry. She now works as a research technician in the Laidlaw Lab and AERD Center and is planning to go to medical school in the future.

**Chongjia Chen, MD**

Dr. Chen is a second-year fellow in Allergy/Immunology at the Brigham & Women’s Hospital. Dr. Chen’s research focuses on the impacts of dupilumab on the immune system in general, and she will be leading the new GLIDER study.