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**MESSAGE FROM OUR DIRECTORS**

With our outreach efforts and enthusiasm from more and more clinicians and researchers in the field, our research collaborations and projects have continued to grow and teach us new insights about this disease. With every new piece of information, we hope to get closer to new treatments as well.

The ENT/Otolaryngology specialty group at BWH has expanded over the last two years, with the addition of several new sinus surgeons who are experienced with AERD patients and severe nasal polyps. This has greatly reduced the wait time for our patients to be evaluated by an ENT specialist when needed. The research group within the Division of Allergy & Clinical Immunology has also expanded, and we now have nearly a dozen researchers who dedicate the majority of their time to investigating the causes of and possible treatments for severe asthma, nasal polyps, and AERD.

Thank you all so much for your continued dedication to this research, and we hope our work serves to answer some of the many remaining questions about AERD.

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

**BY THE NUMBERS**

Our AERD Registry is going stronger than ever thanks to all of you. We are roughly 200 people shy of our goal of 2,000. Based on responses, registry members are 91.1% White, 3.1% are Black or African American, 1.6% Asian, 0.4% Alaskan Native and 2.3% more than one race. 71.5% of participants identify as female and 28.5% as male. Participants are from over 30 countries, including the United States, Canada, the United Kingdom, Australia, Turkey, Norway, Germany, Finland, New Zealand and many more!
RESEARCH HIGHLIGHT: ANOSMIA IN AERD

Outside of clinical trials, another aspect of our research involves examining nasal polyp samples we receive from nasal and sinus surgeries. This year we are highlighting the work done by one of our collaborators in the Division of Allergy and Clinical Immunology, Dr. Lora Bankova, whose research with us focuses on smell.

Patient with AERD often report that their anosmia, or lack of sense of smell, is one of the most debilitating symptoms of the disease. A small area of the nasal cavity known as the cribiform plate contains the vast majority of olfactory neurons, which are nerve cells responsible for our sense of smell. Multiple epithelial cells surrounding the olfactory neurons contribute to their ability to sense odorants but the exact function of these “supporting” epithelial cells is still not clear. A subtype of supporting epithelial cells found in the olfactory portion of both the human and the mouse nose is called a microvillus cell. The microvillus cell has short stubby brushes (“villi”) that extend into the nasal lining fluid (Figure 1).

Although we still don’t fully understand the function of microvillus cells in humans, Dr. Bankova’s studies of mouse noses found that the microvillus cells are sensors of mold and dust mite allergens. In the presence of these allergens, the microvillus cells generate large quantities of cysteinyl leukotrienes, which are pro-inflammatory mediators found at high levels in the nasal fluid of patients with AERD. We are now initiating studies to characterize the microvillus cells in humans and determine if their functions are similar to those in mice. We plan to determine how the inflammatory cysteinyl leukotrienes coming from these cells affect inflammation in the nose and the ability of olfactory neurons to detect odorants.

Figure 1. Microvillus cells (green) surrounded by olfactory neurons (blue stained nuclei) in the olfactory portion of a mouse nose.

PROSTAGLANDIN D2 IN AERD

We are pleased to announce the successful completion of our Prostaglandin D2 clinical study in late 2019. Lead by Dr. Laidlaw, and former BWH AERD Center Assistant Director, Dr. Katherine Cahill, 30 patients with AERD undergoing aspirin desensitization were studied and followed for up to 6 months on aspirin therapy. We collected more than 3000 data points across 4 study visits!

Data analysis is ongoing and findings will be presented at the annual conference of the American Academy of Asthma, Allergy, and Immunology scheduled for February 2021. This results of this study will provide new insight into which patients are at risk for severe reactions to aspirin during desensitization, how 650 mg/day and 1300 mg/day of aspirin affect key inflammatory chemicals in the respiratory tract, and more in the years to come. Thank you to all the study participants for their contribution towards improved treatment for AERD.

AERD Awareness Day 2020

Mark your calendars for September 26th which is AERD Awareness Day! Be sure to purchase your AERD gear from samtersociety.org by August 14th to receive it in time. Proceeds go to support researchers working to better understand AERD.
UPCOMING STUDY: 2-Year follow-up of aspirin-exacerbated respiratory disease registry (“2-FAR”)

This new study, known as 2-FAR, is a 24-month long study that will examine the symptoms and progression of disease in patients with AERD. The study will be conducted entirely online and will not require any additional visits or procedures outside of your regularly scheduled follow-up appointments. We aim to have 100 participants from within our AERD Registry complete a series of 9 sets of surveys, every 3 months, over the course of 2 years. The information gathered from the surveys will help us better understand long-term health outcomes for patients with AERD, as well as how new biologic medications might be beneficial in AERD.

There is compensation of $50 for each completed survey, up to $450 for the completion of all 9 surveys. We expect that each of the surveys will take about 20 minutes to complete. If you qualify, you likely have already received an email from our study team with more information. We are only enrolling the first 100 people who complete the initial emailed registration survey. Please reach out if you have any questions.

In order to take part you must:

- Be diagnosed with or suspect you have obstructive sleep apnea and are not using CPAP
- Be diagnosed with bilateral chronic rhinosinusitis
- Be 18 – 65 years old
- Have a BMI less than 35

For more information, please contact the study coordinator Lauren Hess at 617-732-8976 or lhess1@bwh.harvard.edu.

ONGOING STUDY 2: Ifetroban

As a patient with aspirin-exacerbated respiratory disease (AERD), you know how disabling the reactions and the disease can be. We are carrying out a NIH-funded research study to see if a drug taken by mouth can block aspirin-induced reactions and may help treat AERD. In this study, we will give you the drug or inactive placebo and perform an aspirin challenge. The study involves 3 visits over 8 weeks. You will be compensated up to $225 for participating in the study.

If you are interested in hearing more, call the Asthma Research Center at (617) 732-8201 or email Dr. Tanya Laidlaw at tlaidlaw@partners.org.

Ongoing Study 1: Dupilumab in Sleep Apnea

Researchers at Brigham & Women’s Hospital seek volunteers with obstructive sleep apnea and bilateral chronic rhinosinusitis to participate in a research study investigating how a medication may improve sleep apnea in some patients. The study involves a screening visit, a home sleep test, two overnight stays in our sleep physiology laboratory, two CT scans, and two follow up visits at the clinic. You will receive up to $800 total for participating in this study, and will be treated with dupilumab for 4 months.

Dupilumab/Dupixent in AERD

We continue to see remarkable improvement in asthma and nasal polyps symptoms in patients using dupilumab/Dupixent. Data from clinical trials showed that after 6 months, participants saw over 50% improvement in nasal congestion and obstruction compared to less than 20% improvement in participants who were on placebo. Some benefits included reduction in polyp size, improved sense of smell, and improved asthma symptoms.
Here at the Brigham and Women’s Hospital, we are working on a prospective study to understand how dupilumab/Dupixent works specifically in patients with AERD. Our results so far are consistent with those reported. If you are in the Boston area, considering Dupixent as treatment and are interested in participating, contact Deborah Gakpo (dgakpo@bwh.harvard.edu). We are also looking into comparing how different biologics vary in treating AERD symptoms. Before Dupixent, biologic options included Fasenra, Nucala, and Xolair. We’re interested in understanding why some work better than others for AERD symptoms.

COVID-19 and AERD

The first half of 2020 found us navigating a pandemic due to COVID-19. Although the infection levels remain steady in the Northeast, we see numbers rising in other parts of the United States. The best way to limit spread is to remain vigilant in taking precautions. We recommend you continue to follow CDC guidelines. This includes washing your hands frequently, practicing physical distancing, cleaning and disinfecting commonly used surfaces, wearing masks when recommended, and avoiding touching your face, nose and mouth.

We encourage those with asthma to remain on all medications as discussed with your medical provider. There continues to be no evidence that proper use of asthma medications increases risk of contracting COVID-19 or developing more severe COVID-19. We recommend maintaining routine follow-up with your medical provider through telemedicine or in-person appointments as needed.

We currently have a project underway looking at changes in the levels of receptors for SARS-CoV-2 in the nose, the virus that causes COVID-19, in patients with AERD who are on and off aspirin. In addition, our group was involved in a study published earlier this year that examined where in the body COVID-19 receptors exist, which included analysis of nasal polyp tissue from patients with AERD (Ziegler et al. Cell 2020). Thank you for your continued contribution to research and helping us learn more about how to combat this new virus.

NEW STAFF

Dr. Jyotsna Mullur

Dr. Jyotsna Mullur is a second-year fellow in Allergy & Immunology at Brigham and Women’s Hospital. After graduating from Brown University with a degree in neuroscience, she earned her doctorate of medicine degree from the University of Massachusetts Medical School, and completed a residency in Internal Medicine at Brigham and Women’s Hospital. Dr. Mullur’s research focuses on the impact of biologic medications on clinical outcomes and healthcare utilization in AERD. She will be running the upcoming 2-FAR Study.

Jonathan Hacker

Jonathan graduated this May from Hamilton College where he majored in the Neuroscience. He joined our team in early June as our team’s lab technician.