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**MESSAGE FROM OUR DIRECTORS**

We went ‘live’ with online enrollment for our AERD Registry in February, which has made participation much easier for patients around the world. Then in April we added a new set of questionnaires and emailed them out to existing participants. We had a tremendous response and hope to use data from these additional surveys to examine new AERD research questions:

1) Is there an association between AERD and other eosinophilic medical conditions?
2) Is AERD associated with ear symptoms?
3) How often are patients with AERD mistakenly exposed to NSAIDs after a diagnosis of AERD has been made?
4) Do patients with AERD get benefit from new drugs targeting eosinophils?

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.

Drs. Tanya Laidlaw, Katherine Cahill, & Joshua Boyce

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**BY THE NUMBERS**

With 587 patients enrolled in the AERD Registry, we are more than halfway toward our goal of 1,000 participants! Our participants come from 48 U.S. states and 9 countries. A closer look at the Registry to date shows:

- Average age at which participants developed nasal polyps for the first time is 36 years
- At enrollment, they’d already had an average of 3 polyp surgeries, with a maximum of 15 surgeries reported.
- Over half of our patients reported that their polyps regrew in 6 months or less after surgery
- Most patients experience decreased/total lack of smell

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AERD INFORMATICS ALGORITHM

The electronic health record (EHR) is an important tool that allows medical professionals to search patient charts electronically. Another benefit EHRs provide is the application of informatics algorithms to diagnose diseases. Given that AERD is, in many cases, missed until months or years after its onset, there is a need for more timely identification of the disease in these patients.

Members of our center developed an algorithm to identify potential adult AERD cases. Applying it to the EHR in the Partners Healthcare System over a ten-year period identified 731 possible patients. After reviewing each patient chart, we found that, the algorithm was 88.7% successful in predicting a diagnosis of AERD. Importantly, 12.4% of the cases it identified were cases of undiagnosed AERD – the patients did not even know they had this syndrome. In terms of its ability to identify known AERD cases, the algorithm missed only 3.7% of patients clinically diagnosed with the disease. Since it had high rates of predicting AERD in EHRs, this type of technology holds promise for improving timely patient diagnosis and treatment at our institution and beyond.

QUICK STATS
> The algorithm positively predicted 88.7% of AERD cases in the Partners Healthcare System
> Of the AERD patients it identified, 12.4% were previously undiagnosed

AERD IN CHILDREN

Although AERD is usually considered an adult-onset disease, there have been occasional cases described in children. In fact, 4.2% of patients in the AERD Registry report that they developed asthma and nasal polyps, as well as reacted to an NSAID medication for the first time, prior to age 18.

To add to the current body of knowledge regarding AERD in children, we described three pediatric cases of AERD (all female; ages 7, 12, and 16). Upon confirmation of the diagnosis via oral aspirin challenge, the patients underwent aspirin desensitization. On aspirin therapy, one patient experienced improvement in her cough, but not her nasal symptoms. Aspirin therapy provided little to no benefit to the other two patients, who instead began treatment with Nucala®.

In the past reported cases of AERD in adolescence, the patients’ symptoms have been mild; yet these patient profiles show that more severe symptoms are possible in pediatric AERD.


PRASUGREL TRIAL

We have just completed the analysis phase of our large AERD trial that tested whether treatment with one month of prasugrel, an anti-platelet medication, could help improve the symptoms of AERD or could prevent the reactions to aspirin. This was the largest trial of its kind (40 patients!) ever to be completed in AERD. It appears as though a small subset of patients did indeed get benefit from prasugrel, and the formal publication is in preparation and should be available soon.

ASPIRIN DESENSITIZATION TRIAL

Though tiny doses of aspirin can trigger a reaction in patients with AERD, daily treatment with high-dose aspirin (650 mg twice a day) is one of the few effective therapies that can delay the regrowth of nasal polyps and improves respiratory function for many of these patients. In order for
patients with AERD to start high-dose aspirin, an aspirin desensitization is required, but we do not yet know how the process of desensitization is achieved or why high-dose aspirin can provide benefit. In order to understand the mechanism of aspirin desensitization and high-dose aspirin therapy, the Mechanisms of Aspirin Desensitization and High-Dose Aspirin Treatment study is being conducted at BWH. Patients participating in this research study have four in-clinic visits. They will undergo an aspirin desensitization and then take aspirin 650 mg twice daily for 8 weeks followed by 325 mg twice daily for 2 weeks. Each visit includes blood and urine collections, collection of breath and nasal fluid, a series of written questionnaires, lung function testing, and an evaluation of sense of smell.

**DUPILUMAB FOR NASAL POLYPS**

Dupilumab (Dupixent®) is an injectable medication that is currently being tested in a clinical trial for the treatment of nasal polyps (the drug has already been approved by the FDA to treat eczema). A previous trial in a small group of patients has indicated that dupilumab was effective in reducing nasal polyps, as well as improving sense of smell and other nasal symptoms. The current study is a multi-site Phase 3 trial, which is the final stage of assessment before potential approval of the medication by the FDA for nasal polyps.

Dupilumab is a human antibody that blocks the IL-4/13 receptor. The purpose is to block pathways leading to inflammation—specifically, pathways mediated by type 2 helper T cells, which play a role in coordinating the activity of various other immune cells.

The recruitment period for this trial worldwide closed at the beginning of July 2017, with results eventually expected by the end of 2018.

**AK001 FOR NASAL POLYPS**

AK001 is another medication being tested in a clinical trial for patients with nasal polyps. The goal of the study is to assess both the safety of AK001 and its efficacy in reducing nasal polyps.

The study medication involves three separate infusions of AK001 (some participants receive a small dose, and others, a larger dose) or placebo. The drug is an antibody that is believed to reduce the activation of mast cells and eosinophils, two types of white blood cells that may play a role in the growth of nasal polyps.

We are finished recruiting patients for this trial at the Brigham and Women’s Hospital. Overall, about 70 patients are enrolled in the trial at sites throughout the continental United States and Europe, with results expected in early 2018.

**DIET CHANGES?**

The trial to evaluate whether changing your diet could be an effective way to decrease the body’s levels of inflammation was recently completed. Indeed we did see some dramatic improvements in patients’ symptoms and reductions in the levels of several inflammatory lipids (leukotriene E4 and prostaglandin D2) in their urine. These patients modified their diet strictly for two weeks by increasing their consumption of omega-3 fatty acids, primarily through fish or fish oil supplementation, and decreasing their consumption of omega-6 fatty acids. These dietary changes could serve as an additional health boost to improve quality of life for patients with AERD. The formal publication is in preparation and should be available soon.
OUR NEW LOCATION

In January of this year, the AERD Center relocated to the recently opened Building for Transformative Medicine (BTM). Containing both labs and outpatient clinics, the BTM is a space for clinicians who are using research findings to develop and implement new therapies for patients facing a variety of diseases. AERD patients participating in our clinical trials will visit the Clinical Trial Hub (CTH), a facility located on the third floor of the building.

NEW STAFF MEMBERS

Marina Palumbo
We are excited to bring on Marina Palumbo to the research staff. She will be coordinating for several industry trials as well as maintaining and updating the AERD Registry.

Joseph Singer
We are also excited to welcome Joseph Singer to our team here at the AERD Center. Joseph serves as a patient coordinator for our aspirin desensitization trials and investigator-initiated studies.