

# How Patient Experiences Should Change Our Approach to Treating Patients with Aspirin-Exacerbated Respiratory Disease

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Aspirin-exacerbated respiratory disease (AERD) is a complex and somewhat mysterious inflammatory syndrome that can frustrate the patient and the clinician alike. Although aspirin desensitization and daily administration of high-dose aspirin is beneficial for most patients with AERD, it is not a treatment that is available to or appropriate for all patients and many patients require multiple medications to manage their symptoms. Despite this, their burden of disease remains high,<sup>1</sup> and little has been known about the perceived effectiveness of the medications we offer. Although AERD is often described and treated as a subset of asthma or of eosinophilic nasal polyposis, the syndrome is distinct enough to warrant more individualized therapeutic modalities. However, the underlying causative mechanisms largely remain elusive, which has made the development of specific targeted therapies nearly impossible.

White and Ta<sup>2</sup> write in this issue of *The Journal of Allergy and Clinical Immunology: In Practice* about patient experiences on living with AERD,<sup>2</sup> defined through the results of a cross-sectional online survey of 190 patients about the effects of AERD on quality of life and about the patients' perception of their medical treatments. In addition to quality of life, they assessed patients' views of the effectiveness of available treatments, the factors involved in the decision to initiate high-dose aspirin therapy, and the sense of AERD expertise observed by patients with the disease. This information has never before been available to clinicians and much of it is surprising and could truly change standard approaches to the treatment of these patients.

Above all, it is crucial for all clinicians to be aware of the serious negative effect that AERD has on patients' quality of life. More than 70% of the patients surveyed reported that AERD had at least a moderate negative effect on their quality of life. Specifically, decreased sense of smell was the top symptom that led to that diminished quality of life, and smell is an aspect that both clinicians and researchers often ignore. In fact, the original

20-item Sino-Nasal Outcome Test, used as a validated measure of rhinosinusitis health status and quality of life to assess treatment effectiveness, did not include a single question about sense of smell.<sup>3</sup> Patients in our clinic routinely lament their loss of smell and report that without smell they feel removed from many of their happiest times—the young father who cried as he realized he would never know the smell of his infant son's hair no matter how closely they snuggled, or the elderly Italian woman who quieted sadly with the understanding that the disease had stolen away her loving memories of her late husband as the memories had been closely tied to the smells of the Mediterranean foods they had cooked together over a lifetime. And although anosmia will rarely lead to increased mortality, it is important that our anosmic patients are aware of the hazards of fire and fumes and take special care to ensure the presence of working smoke and gas leak detectors in their homes. Even if no therapies can be offered at this time to bring back their sense of smell, at the very least thoughtful clinicians should take the time to ask our patients about hyposmia and acknowledge openly that it is not yet a symptom we are very good at treating.

Encouragingly, the study did show that daily aspirin was felt to be the most effective treatment according to patients with AERD, as 91% of the patients who had been on aspirin therapy found it to be effective in controlling their symptoms. However, less than half of the respondents had ever undergone an aspirin desensitization or initiated daily aspirin therapy. Here is an area in which White and Ta have taught us that a well-educated clinician could make a huge difference: half of the patients who were offered an aspirin desensitization had refused it, and much of that reluctance was due to patients' concerns over the long-term safety of aspirin therapy. In fact, daily high-dose aspirin therapy is considered to be quite safe. In a group of 172 patients with AERD who had undergone aspirin desensitization and were treated with 650 mg of aspirin twice daily for a year, only 13% discontinued aspirin because of adverse effects, and gastric pain, which reverses on stopping the aspirin therapy, was by far the most common adverse effect.<sup>4</sup> It is critical that we relay details about this safety profile to our patients as they consider the pros and cons of aspirin desensitization so that they make an informed decision.

In addition, we learn from the study that 28% of the patients found zileuton to be extremely effective (though only 24% of the patients had ever been on zileuton), but only 15% found the leukotriene receptor modifiers to be extremely effective (though almost 90% of the patients had been on one of these medications). Sadly, 35% felt that no medicine had made a difference to their symptoms, though most of these patients had never been on aspirin. These data taken together would suggest that (A) aspirin

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desensitization should be more routinely recommended; (B) zileuton should be recommended more frequently than montelukast, which is currently the opposite of what we are doing; and (C) overall in the field we are doing a very poor job of treating more than a third of these patients.

One of our standard treatments for patients with allergic rhinitis is allergen immunotherapy, which is generally considered to provide symptomatic improvement in more than 80% of the patients who complete it. However, in this study, though 45% of the respondents had been diagnosed with concurrent allergic rhinitis in addition to AERD and were on allergen immunotherapy as adjunct treatment, more than half of these patients did not find the immunotherapy to be effective at all, and only 8% found it to be extremely effective. This is a much higher “failure rate” than we are used to seeing in our patients with allergic rhinitis. These data may suggest that patients with AERD have such severe nonallergic nasal and respiratory symptoms that any component due to allergen exposure is overshadowed by symptoms induced by mechanisms underlying their AERD. Regardless of the explanation, clinicians should exercise more caution in choosing which patients with AERD are recommended for

allergen immunotherapy—patients who report no seasonal variation or no identifiable environmental trigger for their symptoms may not be the best candidates.

Finally, it was disheartening to learn, though important for the clinician to know, that one third of the respondents with AERD did not think that their physician was knowledgeable about AERD and turned instead to either social media sites or their own medical literature review. This implies that as a field, allergists need to be doing a better job of educating ourselves and our trainees about this frustrating disease.

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