

The allergic allergist behaves like a patient



A complete disconnection is often seen between the physician's prescription and the patient's behavior for the treatment of pollen-induced allergic rhinitis (AR). Most allergists prescribe medications for the entire season, recommending that the patient should use them regularly, even during days with few symptoms. Conversely, most patients use their medications on demand when their AR is not well controlled and do not follow guidelines.^{1,2}

One neglected question is the attitude of the allergist when he or she is a patient.

During more than 30 allergy meetings around the world for the past 3 years, one of us (J.B.) always asked the same questions: (1) "How many of you have allergic rhinitis?"; and (2) "How many of you use a regular medication during the entire pollen season?" In all meetings in more than 15 different countries globally, the answer was highly consistent. Fewer than 5% of physicians reported using a regular treatment, confirming real-life data recently observed using the MASK app.^{2,3}

To have a well-defined answer, we used a trackpad to assess the questions during the Symposium of the European Academy of Allergy and Clinical Immunology, May 27, 2018, in Munich, Germany. The meeting was attended by approximately 400 allergists, with 102 reporting that they had AR (Table 1). No one used medications regularly. This very limited study confirmed the overall impression from the past 30 meetings that when allergists have rhinitis they are no more adherent to the treatment than patients. Thus, physicians behave like patients when they treat their own AR and do not follow the prescriptions they have written.

This study may help to better understand the poor adherence to treatment in AR and to propose a change management strategy. Health literacy is an important component of adherence to medications.^{4,5} However, in allergists who are highly knowledgeable about the disease, other factors appear to be more important. Physicians often want to hide their own illnesses, but this does not appear to be the case for AR, which is so common that most allergists do not believe it is even a disease. It is possible that human nature drives adherence to treatment regardless of whether the patient is a physician. Physicians and patients are human beings first and foremost and follow the cultural, legal, or regulatory context with similar behavioral patterns. Although a person may have the knowledge and the skills to follow a treatment regimen, and also the confidence (as in the clinicians surveyed), adherence will be low unless a behavior is habituated.⁶

Behavioral science is important in medical care. We need to better understand patients' behavior to propose adequate and

optimized measures of education to improve treatment adherence.⁷ We certainly should see patients' behavior not as a problem to be fixed, but rather as a trustworthy source of information. Methods, techniques, and new mobile technologies⁸ are to be embraced as gateways for this needed understanding so that we might build future treatments based on actual outcomes rather than on hopes and wishes.

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Table 1
Responses Obtained During the Meeting

• Total number of respondents to a generic questionnaire on allergy: 248
• Number of respondents answering the question: "How many of you have allergic rhinitis?": 102
• Number of respondents answering the question: "How many of you use a regular medication during the entire pollen season?": 0

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Severe asthma with eosinophilic gastroenteritis effectively managed by mepolizumab and omalizumab



Eosinophilic gastroenteritis and asthma are typically treated with systemic corticosteroids in severe cases, but chronic corticosteroid use often leads to serious long-term adverse effects.¹ We report a unique case in which eosinophilic gastroenteritis, esophagitis, and severe asthma refractory to systemic corticosteroids was and is being effectively managed by mepolizumab and omalizumab.

A 67-year-old woman presented with a history of childhood asthma that gradually worsened to severe asthma around the age of 58 years. In 2013, this patient visited the emergency department 7 times and was admitted 6 times because of asthma exacerbations. She had chest tightness, cough, dyspnea, occasional headache, and sinus symptoms with purulent nasal discharge and fullness. She also had, approximately every 2 months, intractable nausea, vomiting, and diarrhea that would lead to emergency visits. In 2014, her forced expiratory volume in 1 second (FEV₁) over forced vital capacity (FVC) was 0.47, FEV₁ 1.71 L (71.67% predicted), and FVC 2.5 L (81.66% predicted). Test results for both perinuclear antineutrophil cytoplasmic antibodies and cytoplasmic antineutrophil cytoplasmic antibodies were negative, in addition to skin prick test and serum negativity to *Aspergillus fumigatus*. Her skin testing showed a positive reaction to dust mites and ragweed and was negative to *Alternaria*, *Cladosporium*, *Penicillium*, tree, grass, and animal dander. Quantitative immunoglobulin (Ig)G, IgM, IgA, and IgG subclasses and alpha-1 antitrypsin were not remarkably out of range. Her IgE in 2013 at the time of presentation was 1,236 KIU/L, and eosinophil levels taken at this time and 1 month later were 230 and 400 × 10⁶/L, respectively. She was diagnosed with eosinophilic esophagitis and gastroenteritis, because her biopsy results showed 40 to 50 eosinophils per high-power field, respectively. Eosinophils were found in the lung and sputum. The patient complained of vomiting and diarrhea caused by gastrointestinal (GI) symptoms, but she maintained stable weight. With the aforementioned, she was believed to have had a component of allergic asthma.

To relieve her asthma and GI symptoms, she was prescribed oral prednisone and steroid inhalers. Prednisone dosage ranged from 0 to 50 mg daily between 2013 and 2016, depending on symptoms. Several attempts to taper prednisone were not successful because of persistent asthma and GI symptoms. She received fluticasone/salmeterol, fluticasone, salbutamol, ipratropium, budesonide/formoterol, ciclesonide, budesonide, acclidinium, and montelukast but stopped most of them after at least a 2-month trial because of lack of efficacy. The inhaled steroids were at maximum doses as per the Canadian Thoracic Society 2012 Asthma guidelines.² Although she was adherent to the 6-food elimination diet, she was still dependent on prednisone for GI symptoms, and blood eosinophil counts remained high (eosinophil percentage, 9.4%; absolute, 710 cells/μL). Panel testing of 50 common food allergies was entirely negative with appropriate positive control.

She started mepolizumab in March 2016, at which point her serum eosinophils were 790 × 10⁶/L and IgE was 1,110 KIU/L. Mepolizumab was chosen to target what was thought to be an overall net benefit to the patient, with eosinophils driving both the GI symptoms and asthma. She received 100 mg mepolizumab subcutaneously once every 4 weeks without any noticeable adverse effects. By November 2016, eosinophilic gastroenteritis was effectively controlled with mepolizumab. However, her asthma symptoms were unabated, with persistent wheezing, chest tightness, and chronic cough. She was taking fluticasone/salmeterol 250 μg 2 inhalations twice daily, glycopyrronium 50 μg 1 inhalation once daily, and salbutamol as needed (approximately 6 inhalations daily on average) at the time. Her spirometry in September 2017 showed that her airway was obstructive: FEV₁ to FVC ratio of 0.66, FEV₁ of 2.01 L (71% predicted), and an FVC of 3.05 L (85% predicted).

Because of recurrent asthma exacerbations in fall thought to be related to ragweed, 300 mg omalizumab was added to her regimen in October 2017. This was off the dosing monograph range and was chosen at the physician's discretion. She has received 10 injections since then without any health concerns. Two weeks after the first injection, her respiratory symptoms improved dramatically. She experiences minimal wheeze and mild dyspnea, and she reduced her use of salbutamol to 3 or 4 puffs per week. She is no longer dependent on prednisone for any symptoms.

In allergic asthma, both allergic response and eosinophil activation are reliant on type 2 helper T cells (T_H2).¹ When the airway encounters allergens, T_H2 promote the production of IgE, which in turn binds to leukocytes to release inflammatory cytokines.³ Activated T_H2 themselves secrete interleukin 5, which induces eosinophil maturation. When migrated to the lung mucosa, the eosinophils contribute to airway remodeling.¹

Mepolizumab is a humanized monoclonal antibody that inhibits interleukin-5. Mepolizumab has been shown to be effective in reducing eosinophil levels in serum in eosinophilic GI disorders,⁴ in esophageal biopsy specimens, and in serum in eosinophilic asthma.⁵ Omalizumab binds free IgE and is indicated for allergic asthma.⁶ Whether omalizumab has efficacy in eosinophilic esophagitis or gastroenteritis is not clear.⁷

Because mepolizumab has a distinct mechanism of action from omalizumab, using both biologics may have a synergistic effect if a patient has both eosinophilia (visceral and peripheral) and allergic asthma. Possibly mepolizumab treated the visceral GI eosinophilia while the omalizumab treated the allergic asthma. Another explanation is that although eosinophilia contributed to asthma pathogenesis, her allergic response was equally important in inducing respiratory symptoms irrespective of mepolizumab's effect on airway eosinophils.

Previous studies reported that initiation of omalizumab therapy may unmask underlying diseases, including an eosinophilic disease, Churg-Strauss syndrome.^{8,9} This suggests that when multiple diseases are present simultaneously, single biologic therapy may not be sufficient to treat all symptoms or conditions. Our case supports the idea that multiple biologics are an option if the patient is refractory to