Point-of-Care Testing Pays Off

The Doctor’s Allergy Formula provides ophthalmologists — for the first time — with a comprehensive diagnostic system to identify the root cause of ocular surface disease through non-invasive allergy testing.
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Ocular Surface Disease (OSD) is one of the most common pathologies we encounter. Approximately 50% of patients with OSD have primary or coexisting ocular allergies. Allergies affect approximately 60 million Americans, of which 40% (25 million) have allergies that are ocular in nature.

Proper diagnosis and management is paramount. Left untreated, ocular allergies can significantly affect a patient’s daily life and may result in ocular surface damage. Fortunately, new diagnostic tests have been developed to objectively diagnose and more appropriately direct the treatment of ocular allergies.

Why Do So Many Patients Have Ocular Allergies?

Dr. Trattler: We all have busy practices, both medically and surgically. It’s a bit surprising how often patients come to us with symptoms and signs of ocular allergies, whether as a primary or secondary reason. Please share your thoughts on why we see so many patients with ocular allergies in our practices.

Dr. Luchs: From a demographics standpoint, allergies are serious business. According to some sources, allergic disease affects 30% of the U.S. population. So, there are a large number of people out there with ocular allergies. Allergies are one of the most common conditions with which patients present. They are often a component of a patient’s other OSD manifestations, such as blepharitis, and complaints associated with dry eyes, such as grittiness, burning and uncomfortable eyes. Some patients also complain of itching, or what began as itching and has progressed into irritation and discomfort. Allergies, in general, can affect patients’ lives in profound ways. For example, allergies can affect their ability to read, drive, perform work-related activities and leisure activities, use computers, wear contacts lenses and so on. So, it’s important that we make the diagnosis and treat patients quickly once we’ve determined ocular allergies are present.

Dr. Parekh: Furthermore, as ophthalmologists, we’re poised to see allergy patients throughout the year, versus allergists who tend to see patients only during the two big allergy seasons: pollen in the spring and ragweed in the fall. Allergy has a huge overlap with dry eye, blepharitis and contact lens overwear syndrome. We see many allergy patients, and a good deal of them complain of itch, foreign body sensation, and red, watery, scratchy eyes. And it’s really important to go through the differential diagnosis. Again, allergy can take many forms: perennial, seasonal, atopic keratoconjunctivitis (AKC), vernal keratoconjunctivitis (VKC) and giant papillary conjunctivitis (GPC). It’s our job to rule out other potential reasons for the symptoms, so we can arrive at a differential diagnosis of ocular allergy.

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Dr. Malhotra: There’s a huge Venn diagram of overlap between OSD with allergies, dry eye, blepharitis and ocular rosacea. It’s usually not just one disease, but an overlap of multiple diseases. It’s critical to remember that treatment of one could affect treatment of another. Many patients are self-medicating or their primary care doctor may prescribe oral allergy medications year-round, which can make dry eyes worse. So, addressing their allergies, or lack of allergies, could sometimes improve their symptoms. OSD can routinely affect vision. It affects our surgical outcomes with LASIK, refractive and cataract surgery. That’s why we often find that dissatisfied surgical patients have ocular surface disease.

Dr. Luchs: Often, it’s not just one ocular surface disease. There can be several. And it’s important to address what you think is primary, while not neglecting anything else that may be present.

Who’s Experiencing Ocular Allergies?

Dr. Trattler: Are there any groups of patients that are at higher risk for experiencing ocular allergies?

Dr. Malhotra: If patients have poor, insufficient tear film or rapid tear breakup time, it can exacerbate allergic symptoms. I always think of it like a razor burn. You have friction on your eyelid, you don’t have adequate tear film and you develop some bumps on the inside of the eyelid from friction and that can create papilla. There are also chemical mediators...
associated with the papilla. I think patients like diagnostic tests, because they want to see objective evidence to confirm our diagnosis.

**Dr. Pepose:** I don’t think we see allergies in really young children, up to age 2 or 3, as frequently because they haven’t had long enough to be sensitized. We see vernal in the next age group, 4 to 12 years old, particularly in boys, and it’s more common in warm climates. Allergies can occur in individuals across the board, particularly in atopic patients who are genetically predisposed anyway. They have eczema; they have asthma.

**Dr. Malhotra:** When you ask patients if they have allergies, approximately 80% to 90% of them say ‘yes’ — even when no one has formally diagnosed them.

**Dr. Parekh:** Ocular allergies can go very much ignored. Patients don’t just self-diagnose, they self-treat. They’re all using OTC antihistamines now, and if they have dry eye, they’re actually exacerbating their symptomatology.

**Dr. Trattler:** Dr. Loff, could you comment on what led you to develop an objective way to diagnose allergic conjunctivitis?

**Dr. Loff:** As a practicing ophthalmologist in Georgia, I was one of the leading prescribers of Patanol (olopatadine hydrochloride ophthalmic solution 0.1%, Alcon). I found it very frustrating because I was evaluating patients with OSD but I didn’t know exactly what the underlying pathology was, so I was forced to use a shotgun approach, recommending various drops until the patient found some relief. If symptoms did improve with the drops, I knew we were really just masking the symptoms — not getting to the root cause.

With that in mind, I worked with some of the leading botanists to develop specific, regionalized allergy panels for each part of the United States to determine the most ocular-specific allergens, which, for the first time, can truly objectively quantify and qualify the root cause of specific underlying ocular allergies. With the Doctor’s Allergy Formula (DAF) system, we’re finding that approximately 95% of patients tested have a positive response to at least one allergen. For the 5% of patients who don’t respond, the test allows us to rule out ocular allergies, so we can focus on identifying other causes of OSD. I look forward to hearing everyone’s feedback and experience on their use of the system.

**Types of Ocular Allergy**

**Dr. Trattler:** Let’s discuss the types of ocular allergic conditions, including seasonal, perennial, vernal, atopic and GPC.

**Dr. Pepose:** Sure. You think of seasonal allergies as being mostly in the spring and summer maybe in some part of the country extending into the fall. Those would be trees, and grasses, and pollens — ragweed, for example, would be a perfect example. That might be temperature dependent, too. It might be a seasonal thing. If you have a warm season, you might have a higher pollen count, for example. In terms of perennial allergies, we’re talking about household allergens, things you’re exposed to all the time, such as mites, dust and pet dander.

**Dr. Parekh:** Vernal conjunctivitis is more common in males by a ratio of about 3 to 1 and often occur in children ages 4 to 12. Vernal conjunctivitis is also more common in warm climates.

**Dr. Luchs:** The main concern about vernal and AKC, the least common but potentially the most

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– Jai G. Parekh, MD, MBA
severe of the allergic diseases, are the potentially sight-threatening complications, such as shield ulcers, and the potential for almost a pemphigoid like migration of the ocular surface in patients with atopic keratoconjunctivitis — all of which can be quite devastating. But I think what distinguishes these two conditions from the seasonal is that vernal and AKC are really disorders of the immune system. They are defects within the regulation of the T & B cells.

The Inflammatory Cascade

Dr. Pepose: The inflammatory cascade starts with dendritic cells presenting the allergen. The ocular surface has different types of antigen-presenting cells: Langerhan cells and macrophages. They’re going to present the antigen to naïve T cells, which then become activated and become T-helper (TH) cells and then the TH cells turn on B-cells to produce the IgE, creating sensitization and IgE release.

The IgE is then bound by the mast cells so the next time the allergen is presented, you’ll now have sensitized mast cells because they have surface IgE and they’re going to degranulate. The histamine is already preformed, so there is an immediate release of histamine and then you start to turn on production of leukotrienes and prostaglandins, which is part of the arachidonic pathway. That’s the next stage — the early stage.

The later stage would be recruitment of other cells via the release of cytokines, which
up-regulate adhesion molecules, such as ICAM, and there is also the release of neuropeptides. Eventually, you begin to see migration of eosinophils and T-cells and macrophages. That’s when the chronic stage of inflammation begins.

**Dr. Luchs:** To put it simply, for sensitized individuals, there are antigens in the air. They dissolve in the tear film, where they can gain access to the mast cells in the conjunctiva that have already been coded with the antigen specific IgE. The antigen binds to those IgE receptors and the mast cell causes degranulation. Histamine releases as well as all those other inflammatory mediators. Histamine binds to the nerve endings of the conjunctiva, which causes itching. It binds to the histamine receptors in the vasculature of the conjunctiva to produce vasodilation and increases in vascular permeability, which cause redness and swelling. That’s the basic triad of the itch, the redness and the swelling of the allergic response.

**Dr. Malhotra:** When I have an ocular surface disease patient and I’m trying to differentiate, I’m looking for chemosis and papilla. If I see any chemosis or papilla and any of suspect symptoms, then I’m going to order allergy testing.

**Allergy Triggers**

**Dr. Trattler:** Let’s discuss how allergy skin testing has affected the way you evaluate and treat patients.

**Dr. Malhotra:** Dr. Loff, when using Patanol, did you have patients use it seasonally or year round?

**Dr. Loff:** Well, if we assumed the issue was seasonal, I had them use it during a specific season. But again, without truly knowing what a patient was allergic to, it was a very frustrating process from my perspective.

**Dr. Malhotra:** With the results of an objective allergy test, you know when patients most need medication, so they don’t have to use it year round, which potentially saves patients money. Also, you can better help patients avoid their triggers. For example, if a patient is allergic to feathers, have him get rid of down comforters and feather pillows. I have several patients who had chronic atopic lid disease. Allergy testing revealed that they were allergic to feathers or dust mites. Once they know and can avoid the offending allergen, they’re essentially cured and can stop taking medications.

**Dr. Parekh:** Behavioral modification is very tough to institute if you don’t know what a patient is allergic to.

**Dr. Luchs:** It’s really eye opening to think about the number of patients we see who answer ‘yes’ when you ask if they have allergies, yet they have no idea what
they’re allergic to and they’ve never undergone allergy testing.

**Dr. Malhotra:** The majority of the testing panel given by allergists is for food allergies. It’s not for the most common ocular allergies. So, some patients have been told they don’t have allergies, but it’s because the test wasn’t specific to their allergen. And that’s another big advantage of Doctor’s Allergy Formula testing — the regionalized panel of this ocular specific allergy test.

**Dr. Loff:** I agree. One reason I created the test is because I found it frustrating when I sent patients to an allergist and they were tested for the wrong things — allergies to medications, foods and insect bites. Patients are fearful about needles and shots. It’s a very uncomfortable process. This also drove me to develop an ocular-specific program that was noninvasive, without any shots or needles. It is very simple for any ophthalmic practice to implement this test in the office.

**Increased Testing in Eye Care**

**Dr. Pepose:** I think we’re seeing a paradigm shift in the way ophthalmic care is delivered. We’re going to be providing more point-of-service testing. We already have tear osmolarity. We have new tests such as MMP9. We’re going to have IgE testing as part of an initial screen for allergies, so we’ll become more like internists in some ways. But instead of using blood for analysis, we’re going to use tears. This profile is going to orient us in a certain direction. Additionally, one of the missing components has been skin testing to get some specificity and we now have the ability, with sublingual immunotherapy, to actually treat these patients without shots. We’re going to practice evidence-based medicine as a new standard of care. And I think that’s good for everyone.

**Dr. Trattler:** It certainly is exciting to have the ability, for the first time, to determine the specific allergens that are affecting our allergic conjunctivitis patients.

**Dr. Luchs:** It takes some skill and a bit of art to determine what’s going on with some patients. And that’s where a point-of-care test is ideally suited to help guide our diagnoses and treatment recommendations. Allergy skin testing can be very helpful in sorting out what contribution allergy is causing to a patient’s OSD or whether it’s contributing to their ocular surface complaints.

**Dr. Malhotra:** We know that dry eye patients also may have allergic conjunctivitis and that the two are not mutually exclusive. With allergy skin testing, we can start to delineate the underlying pathology, and tests for lactoferrin, MMP-9 or IgE may also be developed.

**Dr. Trattler:** Being able to test for a specific allergen allows us to direct our therapy and treatment recommendations. It’s interesting that many patients believe they know what they’re allergic to, but test results often surprise them. For example, we have a technician in our office who thought she was allergic to dogs. Based on our testing she’s not, so now she can interact with dogs without fear of an allergic reaction.

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— Ranjan Malhotra, MD
Efficient Testing

**Dr. Pepose:** In terms of efficiency, one of the nice things about this test is that we don’t have to perform it ourselves. A nurse practitioner, physician’s assistant or other office tech often can handle this step. Then you receive the results and provide the counseling.

**Dr. Luchs:** I’ve begun to integrate it into my protocol for anyone with ocular surface disease to help determine what, if any, contribution there is to allergy. It may reveal that the patient does in fact have an allergy and that it’s playing a major role in their ocular surface disease.

**Dr. Parekh:** Proprietary testing with Doctor’s Allergy Formula works well because it’s noninvasive — no needle or shot is required. I haven’t had a single patient resist the workup. If during my workup, the patient has hyperactive airway disease, rhinitis or eczema, I refer him to an allergist for a further work-up. I’ve found that in some parts of the country that allergists are quick to rush these patients to immunotherapy when often, all they have is localized ocular disease.

**Dr. Pepose:** I’ve found that only a small percentage of patients, maybe only 5%, are electing to go through sublingual immunotherapy to create tolerance to the allergen — although it’s certainly more appealing for them not to have any shots. And the skin test itself is not a shot, it’s just a plastic roller, rolling to scratch the skin, so it’s not invasive.

**Dr. Parekh:** If testing indicates it’s simply an ocular allergy, I can change the therapeutic regimen,

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Exacerbating Behaviors

**Dr. Trattler:** Dr. Pepose, can you discuss the “hygiene hypothesis”?

**Dr. Pepose:** Yes, it’s a hypothesis that’s been around for a long time. It was based on clinical observations that on average, there were less allergies in people with larger families and also those who grew up on a farm rather than in the city. The hypothesis was that in the large families, you’d get more exposure to infectious diseases than in small families. In the same sense, as countries became more developed, there was better hygiene. This lack of exposure to normal commensal microbes didn’t dampen one’s immune response and induce tolerance, which normally would occur because these microbes were around so much. I think that’s the general hypothesis.

**Dr. Trattler:** One important topic to mention is keratoconus, as this condition is associated with ocular allergies. Patients often are eye rubbers and underlying allergies can lead to the development and exacerbation of keratoconus.

**Dr. Malhotra:** Plus people who have obstructed sleep apnea often have dry eye. Almost every single one of my patients that come in with keratoconus has allergy testing, and it’s something that I address. Even if you crosslink them, you need to address their ocular surface. As you know, keratoconus is associated with ocular allergies, and you want to keep patients from rubbing their eyes because even if you crosslink them, it could still develop into a progressive disease. So, I think that addressing that component is important and finding out if they’re allergic to something that’s avoidable is extremely important.

and the patient can work on behavioral modification, use a HEPA filter, avoid pollen, dander or whatever it may be, and return in a few months for follow up.

I’ve been performing this test for several months and the results are quite impressive. Patients return 1 month after we’ve done the test, hopefully having made some of the recommended changes and I would say 80% feel better. Immunotherapy isn’t the only solution for these patients, and it’s certainly not first-line therapy.

### Potential Risks

**Dr. Trattler:** Is there anything to consider before patients undergo this test?

**Dr. Luchs:** There’s a very small risk of anaphylactic reaction to an antigen, but the antigens being evaluated are environmental, so they’re things most people are exposed to in everyday life. Thus, the likelihood of an anaphylactic reaction is extremely remote.¹³

**Dr. Parekh:** Though the risk is low, it’s important to have EpiPens or other medications, such as Benadryl (diphenhydramine) and oral sublingual antihistamines, on hand to help mitigate any kind of reaction. There have been a couple of reports of localized reactions on the skin, but nothing systemic.¹³

**Dr. Loff:** As Dr. Luchs mentioned, the Doctor’s Allergy Formula test is specific for environmental allergens that most people are exposed to regularly. There’s never been a reported serious adverse or anaphylactic reaction with any of the allergens tested with our system.

### Pre-Testing Protocol

**Dr. Trattler:** What’s your protocol for patients prior to testing?

**Dr. Pepose:** I give patients a list of medications they should avoid prior to testing. They have to stop nasal and topical ocular antihistamines 48 hours in advance. For oral antihistamines and some antidepressants and sleep medications that have antihistamine effects, patients are instructed to stop taking them 5 days before the test.

**Dr. Parekh:** We take the patients in the examination area, which is the allergy room now, and my technician performs the test. The patients go back to the waiting room and watch television for 15 minutes, then return to the room and have the test read. I review the results and counsel the patient before he leaves. We’ve streamlined the testing process so it takes only 35 minutes total.

We actually earmark a couple of sessions throughout the month as sessions for allergy testing. The whole office is turned into an ocular allergy practice and the turnaround time is terrific. The patients come in for testing and then counseling from me. I usually tell them to avoid certain behaviors or activities that put them in contact with allergens, and then we follow up in a month to see exactly how things are progressing. Not one patient, and we now test several hundred patients in our practice, has been resistant to undergoing this test. Not one.

**Dr. Pepose:** Because the allergens are applied using a plastic applicator, patients have a very different response than if we’d approach them with a needle or tuberculin syringe.

**Dr. Malhotra:** Some patients think they have to be tested when their allergies are acutely occurring. So it’s important they understand they can be tested any time because we’re exposing them to an allergen to which they’ve already been sensitized.

“As an ophthalmologist, I was frustrated with the shotgun approach utilized in subjectively diagnosing ocular allergies. This motivated me to develop a specific ocular-oriented program that was noninvasive — without shots or needles — that was also very simple for any ophthalmic practice to use in their office.”

> – Howard J. Loff, MD
Dr. Loff: It’s also important to note histamine control. Many doctors find that if the histamine response is minimal (less than 4 mm), patients respond better to steroids as the primary option in lieu of antihistamines. For those patients who have a moderate (4 to 6 mm) or exacerbated response, it’s better to recommend antihistamines because they’re more likely to respond to those. So, the test, used in conjunction with the histamine response, can help direct which pharmacotherapy would be best for a specific patient.

Conclusion

Dr. Parekh: Finally, I’d like to mention that Doctor’s Allergy Formula testing uses a multidisciplinary diagnostic code, so it’s not a lab test. We’re not the first practitioners to do this. Allergists, dermatologists, even some primary care doctors are doing this so we’re actually late to the game.

Dr. Luchs: This test streamlines caring for our patients because in one or two visits, they can have their ocular surface complaints sorted out in one location — from allergy to dry eye to blepharitis — rather than self-medicating, seeing an allergist, seeing their primary care physician doctor for red eye and possibly getting an antibiotic. When ocular allergies are the main problem, we can handle their medical care.

Dr. Parekh: This test is apropos for the healthcare climate we’re in because it is truly point-of-care testing. And when so many other tests don’t pay enough but yet we feel we owe it to our patients, this is actually fits really well in the model of how best to take care of patients.

REFERENCES
