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IMPROVING CLINICAL CONFIDENCE

A new paradigm
in determining
the etiology of
conjunctivitis.

Improving Clinical Confidence With Point-of-Care Testing: A New Standard of Excellence for Optometry

Conjunctivitis is a leading reason for patients to present to their eye care doctors. It is estimated that there are around 6 million cases of acute conjunctivitis diagnosed each year,¹ and it is associated with decreased visual acuity, light sensitivity, chronic tear production, visual loss, and subepithelial infiltrates.²⁻⁵ Yet, despite how common complaints of red eyes are, accurately diagnosing the cause remains a persistent challenge. Because identifying the etiology has very real implications for directing therapy, eye doctors need an effective means of differentiating between viral, bacterial, and allergic conjunctivitis.

Numerous studies highlight the significant overlap in clinical signs and patient-reported symptoms between the three most common causes of conjunctivitis.⁶⁻⁸ An inaccurate diagnosis, however, may lead to the improper use of antibiotics, for example, in cases of viral involvement. Clearly, eye care practitioners need a way to improve the odds in their favor.

Enter the Red Eye Protocol and point-of-care testing using the AdenoPlus immunoassay (Nicox, Inc.), the first in-office testing aid for the identification of adenoviral conjunctivitis. Although fast and easy to perform (the four-step protocol can be completed in under 2 minutes, and results are available within 10 minutes), the AdenoPlus Test can detect all known serotypes of adenovirus with 90% sensitivity and 96% specificity. The value of achieving an accurate diagnosis

is manifold. Armed with a definitive diagnosis, clinicians can target therapy to the underlying cause, thus alleviating symptoms faster and more reliably. Not to be overlooked, however, is the confidence that the testing protocol inspires in both patients and their doctors.

At a recent roundtable sponsored by Nicox, a panel of renowned experts assembled to discuss the implications of introducing point-of-care testing with the AdenoPlus into optometric practice. They discussed the many advantages that testing may have, including its potential to help grow the practice, to differentiate in a competitive marketplace, and as a tool to connect optometrists to the larger medical community. But one overarching theme emerged from this panel of experts: The single greatest advantage of using AdenoPlus testing is that it helps optometrists be better clinicians for their patients.

1. Data on file, Nicox Ophthalmic Diagnostics.

2. Sambursky R, Tauber S, Schirra F, et al. The RPS Adeno Detector for diagnosing adenoviral conjunctivitis. *Ophthalmology*. 2006;113:1758-1764.

3. Butt AL, Chodosh J. Adenoviral keratoconjunctivitis in a tertiary care eye clinic. *Cornea*. 2006;25(2):199-202.

4. Hyde KJ, Berger ST. Epidemic keratoconjunctivitis and lacrimal excretory system obstruction. *Ophthalmology*. 1988;95(10):1447-1449.

5. Hammer LH, Perry HD, Donnenfeld ED, et al. Symblepharon formation in epidemic keratoconjunctivitis. *Cornea*. 1990;9(4):338-340.

6. O'Brien TP, Jeng BH, McDonald M, et al. Acute conjunctivitis: truth and misconceptions. *Curr Med Res Opin*. 2009;25(8):1953-1961.

7. Leibowitz HM, Pratt MV, Flagstad JJ, et al. Human conjunctivitis. *Arch Ophthalmol*. 1976;94:1747-1749.

8. Stenson S, Newman R, Fedukowicz H. Laboratory studies in acute conjunctivitis. *Arch Ophthalmol*. 1982;100:1275-1277.

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All are paid consultants to Nicox, Inc.

Paul Karpecki, OD: My staff and I decided to implement The Red Eye Protocol in our practice because we thought it would make us more accurate at making the correct diagnosis. I wanted firsthand experience with this protocol in order to stay ahead of the curve in anterior segment disease. The AdenoPlus (Nicox, Inc.) test, an important element of the Red Eye Protocol, makes this process very easy to put into practice. The test is accurate and quick to perform. It takes my staff about 2 minutes to conduct the test, and I can see other patients while waiting for the results. Once the results are available, after about 10 minutes, I am able to make the differential diagnosis quickly.

I feel that the Red Eye Protocol and the AdenoPlus test help me be a better clinician. I find it amazing that, as a whole, eye care practitioners make an accurate diagnosis only about 50% of the time.¹⁻³ I did not believe that would be the case in my practice, of course; I thought I would be better. However, of the first four patients we saw in our clinic with red eyes and who we tested with AdenoPlus, my clinical diagnosis was wrong 50% of the time.

The reason why diagnosing acute conjunctivitis is so challenging is that quite often, its presentation can mimic multiple potential etiologies. You think you are looking at a bacterial infection, and it winds up being viral, allergic, or even something else. There is significant overlap in the signs and symptoms of different kinds of conjunctivitis.⁴⁻⁶ If you look at the research, discharge and redness are common to both bacterial and viral conjunctivitis.^{4,7-8} I always thought bacterial conjunctivitis involved significantly more infection, especially in the superior region (Figure). Likewise, there is less difference in the purulent discharge between viral and bacterial conjunctivitis as one might think. Some clinical signs are obvious: mucin production is higher in patients with allergic conjunctivitis, although it is also present in viral. Itching is higher in allergic conjunctivitis, but it can also be present in viral and bacterial cases greater than 30% of the time. The take-home message here is that there is a tremendous amount of overlap.

Adenovirus is the most frequent virus isolated on the conjunctiva,⁹⁻¹⁰ representing about 6 million cases a year,¹¹ which indicates that it may be more prevalent than clinicians expect. I think the AdenoPlus test will show us exactly how prevalent adenovirus is. Mile, have you had surprise positive cases of adenovirus that you would have diagnosed as something else?

Mile Brujic, OD: Yes. The patients that have surprised me most are contact lens wearers, where my staff and I thought the irritant was some kind of contact lens infiltrate, but it was epidemic keratoconjunctivitis (EKC). Those cases made us particularly grateful that we had implemented the Red Eye Protocol with AdenoPlus testing to catch the EKC. We used to isolate those patients as separate

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cases, but now we have added contact lens emergent red eyes into our Red Eye Protocol.

David Kading, OD: Do you think we are going to see more adenovirus than we ever thought possible, because we have been misdiagnosing it all along?

Dr. Brujic: We may not currently appreciate the scope of the problem until we start looking for it. If we do begin to identify more adenovirus cases using this protocol, we may learn additional clinical information that helps us to look at this problem more effectively.

POINT-OF-CARE TESTING AS A PRACTICE BUILDER

Dr. Kading: I think the AdenoPlus test has the potential to be a practice builder. Although my staff and I have not actively marketed our use of the test, when parents comes to the office with a child with red eyes, we can now tell them that we have a test to determine if their child can go to school or not. The ability to provide patients with a definitive diagnosis can certainly build credibility for the practice.

Dr. Karpecki: I agree—being able to tell people if they are contagious or not is a very effective service. Are there other groups that might be interested to know that this test allows us to be red eye specialists?

Ron Melton, OD: When health care providers develop a red eye, the first thing they think is that they have a methicillin-resistant *Staphylococcus aureus* eye infection. They also want to make sure the eye infection is not contagious (adenoviral). Therefore, the AdenoPlus should be well accepted by nurses and physicians as it will provide a fast, efficient method of identifying whether the patient has an adenoviral infection.

Dr. Brujic: My staff and I interface frequently with our medical community. We are in the process of writing a form letter letting our colleagues know we have a test that can distinguish between viral and bacterial conjunctivitis, so we become their source for questionable red eyes. We are sending these letters to physicians and educating everybody we can reach.

Dr. Kading: We could also send a similar letter to school nurses explaining that if they see a suspicious red eye, there are local eye care providers with the AdenoPlus test who can pinpoint the source before an infection has the chance to spread.

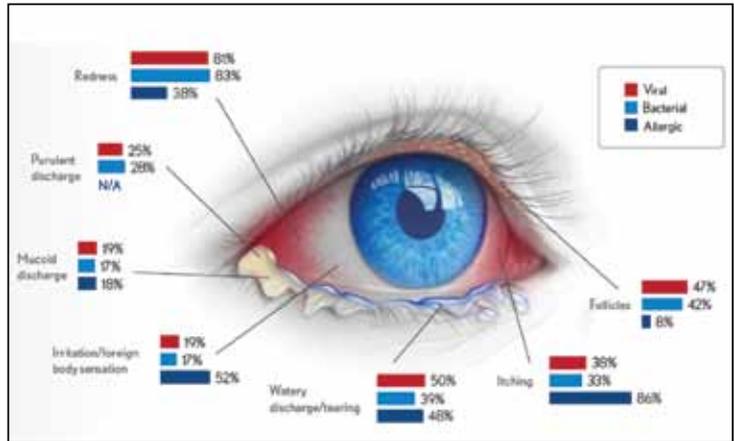


Figure. There is significant overlap in the signs and symptoms associated with the three most common etiologies of acute conjunctivitis.

Art Epstein, OD: Certain bacterial conjunctival entities are contagious, so if you are making a differential diagnosis on EKC versus bacteria, you may not be completely out of the woods.

Dr. Melton: It is true that patients' symptoms often throw you off track. This morning, I saw a woman who had a significant red eye for 2 to 3 days. She said it was "goopy" in the morning, and she could not open it. Clinically, I observed a mild serous discharge. Based on the signs, I was thinking adenoviral conjunctivitis as the diagnosis, but her symptoms made me think it could have been a bacterial conjunctivitis. I recommended the AdenoPlus test, which tested positive for adenoviral conjunctivitis. The test was able to give me an objective finding for the diagnosis.

Blair Lonsberry, OD: To help primary medical practitioners accept this test, it may be analogous to their having a point-of-care test for streptococcal infection and how that relieved both patients and providers in knowing that differentiation.

IMPROVING ACCURACY

Alan Kabat, OD: Sitting here as an academician, I naturally have questions about how this test adds to the clinical practice. Are there aspects to this test beyond its value as a practice builder?

Kelly Nichols, OD, PhD: I think the practice building aspects are important, but that is not the main reason to incorporate point-of-care testing for adenoviral conjunctivitis into the clinic. The primary reason to implement it is because it represents good care—it means being able to give our patients a definitive diagnosis about their eye infection and then creating a targeted plan to treat it. This knowledge will save us and our patients time and money, especially if it can help avoid inappropriate prescriptions.

(Continued on page 6)

Improving Diagnostic Accuracy

During the roundtable, Paul Karpecki, OD, presented some cases that illustrate the confusing nature of conjunctivitis. As the panel of experts discussed the overlap in signs and symptoms, it became obvious that missing the diagnosis could not only lead to poor outcomes, it can erode the trust between a patient and his or her eye care doctor.

Paul Karpecki, OD: This is a case that demonstrates how valuable the Red Eye Protocol is, especially when AdenoPlus (Nicox, Inc.) testing is performed prior to the clinician's examination.

A 31-year-old teacher came to my clinic reporting a red eye for about 4 weeks (Figure 1). There was no apparent upper respiratory infection, but she had positive preauricular lymph adenopathy. I discovered grade 2+ blepharitis in the upper eyelid of both eyes and grade 2 injection in the right eye. I witnessed good follicular response, at least 2+, at the slit lamp. In this case, my technician did not perform the AdenoPlus test before the evaluation.

Given the long-standing infection, female gender, and age of the patient, my clinical impression was that this was likely bacterial, and specifically, chlamydia. Based on this assumption, I asked the patient about her marital status. After looking at me quizzically, she reported that she been married for 6 years. I explained to her that there are certain conditions that involve sexually transmitted diseases, so

I had to ask the medical questions. It was, nevertheless, a little uncomfortable.

When I got the results of the AdenoPlus test back, however, it indicated a positive result with two red lines. It was then that I realized I could have avoided that entire awkward discussion if the test were run first. In another case, a female patient reported to my clinic with red eye for 5 days with mattering in the morning. She noted that it was goopy and more white than yellow. My clinical evaluation revealed clear eyelids with some minimal white debris on the surface of the eye (Figure 2). The eye appeared to be slightly hemorrhagic. The deposits gave me the impression that this was a bacterial conjunctivitis. However, the AdeoPlus test showed two red lines, indicating a positive for adenovirus.

Art Epstein, OD: I think the point that these two cases really demonstrate is that even good clinicians who tend to have accurate clinical impressions are not always right. Essentially, AdenoPlus testing is a foolproof way to know you are not wrong.

Alan Kabat, OD: It shifts the paradigm. If one thinks about a disease state like diabetic retinopathy, the usual course is for the clinician to inspect the retina and then perform testing, like optical coherence tomography, as confirmatory. With this, we are doing the test almost prophylactically.

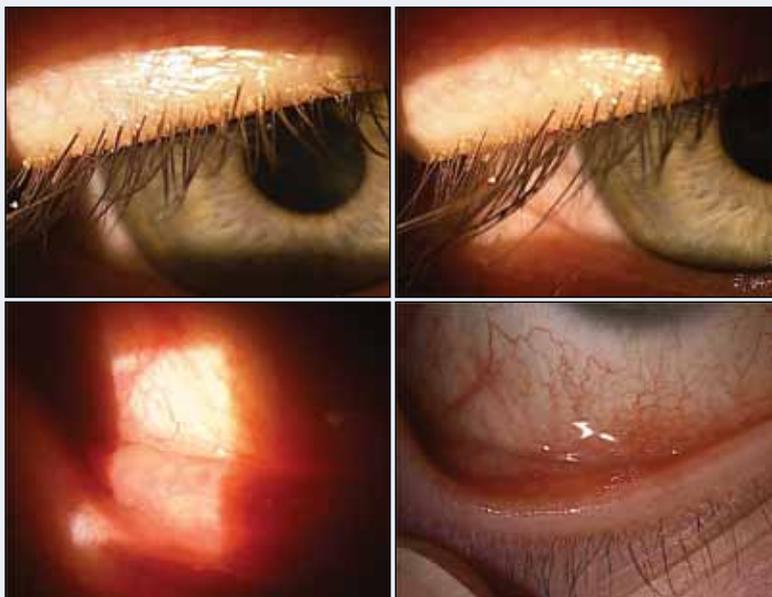


Figure 1. The clinical examination revealed obvious conjunctivitis, but of unspecified origin.

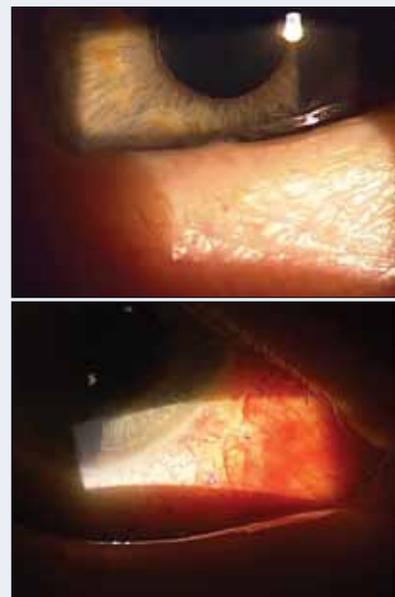


Figure 2. Signs classically associated with bacterial conjunctivitis are also frequently found in viral etiologies, as seen here.

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Kelly Nichols, OD, PhD: Exactly. It is point-of-care testing, similar to how internal medicine practitioners might require a strep and influenza test prior to an examination for patients with suggestive signs and symptoms.

Dr. Epstein: A lot of this is relevant to how we value our time. In the case of the pediatrician using point-of-care testing, he or she does not want to see someone when an examination is not necessary.

Dr. Karpecki: We get 40 to 50 patients a day in my clinic 3 days a week. My goal is to find the ones that can we can process quickly, because that can change the efficiency of my day. This test can help us triage the red eyes quickly and efficiently, and ultimately make us better care providers. If I know what the patient has, I can look at the eye for a few things, and then move on to a treatment decision. The relevant question may be what kind of treatment is good for eyes with positive results in the AdenoPlus test. I use povidone-iodine for some patients. Ron, you have been doing this a lot longer than I have.

Ron Melton, OD: If I am going to do this, I start by making sure as best I can that the patient is not allergic to iodine. The first step in providing the betadine treatment is to anesthetize the eye with one to two drops of proparacaine. After two to three drops of povidone-iodine, the patient is asked to shut their eyes while the clinician rubs any excess betadine into the lids for about a minute. Follow this with a thorough rinsing with sterile eye wash. I like to prescribe a steroid drop q.i.d. for 3 to 4 days after the povidone-iodine flush. The key to success with this treatment is catching the virus in the first 3 to 5 days as it is evolving. If it is a really bad adenoviral infection that has been active for 10 days, using povidone-iodine is unlikely to be of benefit. One reason corneal specialists do not perform the betadine treatment is that it requires chair time, and in a busy practice that can be financially unproductive.

Dr. Karpecki: A positive AdenoPlus result allows me to prescribe Zirgan (ganciclovir ophthalmic gel 0.15%; Bausch + Lomb) for the patient and it is a very quick examination with a little education about the virus and treatment. But I have some patients who cannot afford Zirgan so I would opt for a povidone-iodine rinse in office. Kelly, you said that patients are beginning to expect this type of technology at the point of care in a primary doctor setting. I wonder if you agree that soon, eye care patients will expect this also?

Dr. Nichols: Once they know this is available, they will expect it.

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Dr. Kading: I remember two patients of mine who had a positive result on the AdenoPlus test. Although I was positive I knew that they had adenovirus, even if there is a 0.1% chance that I could be wrong, it is worth checking.

Dr. Nichols: Having this point-of-care test is about good quality care. It is really a different way of thinking about delivering care.

Dr. Lonsberry: Some doctors still use Tobradex (tobramycin and dexamethasone ophthalmic suspension, Alcon Laboratories, Inc.) or Zylet (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension, Bausch + Lomb) on almost all patients who present to their offices with red eyes, because they want to feel good about putting the antibiotic over top of it. This is another reason why homing in on the diagnosis is so important, because if you are certain it is viral, then you know that antibiotics are inappropriate.

Dr. Karpecki: This is an important point: implementing point-of-care testing for adenoviral conjunctivitis with the AdenoPlus is good medicine. It is valuable because it allows practitioners to follow recommendations for evidence-based medicine.

Doug Devries, OD: Every practitioner in the room using this test remembers misdiagnosing a patient. If the high-caliber physicians in this group can make that mistake, imagine the improvement in diagnostic accuracy we can expect once the community at large adopts the test.

Dr. Nichols: This past winter, my family got sick from influenza. I did not know we had influenza, but I knew we were all sick. The school nurse called and said one of my kids had an ear infection and suggested we go to the doctor. I made an appointment for all of us to go, and the first thing they did was run two tests, for streptococcal infection and for influenza. As it turned out, we all were positive for the flu.

There are a lot of similarities with the Red Eye Protocol in terms of the process for differentiating for influenza. The first tests my family underwent when we visited the primary care physicians were two rapid assays before seeing the doctor. Thus, point-of-care testing is an accepted—and expected—as standard nowadays. Why should it be any different for patients with red eyes in our practices?

Dr. Melton: When my sister got sick, she went to a Walmart walk-in, and they did the same thing. This kind of point-of-care testing is standard care in general medical practice.

Dr. Epstein: Knowing the differential is important. In the case of strep throat, antibiotics are a likely choice for treatment by most physicians. But if it is influenza, then obviously, that would not be the case. I think many optometrists believe they do not need to know the cause of a red eye, because a combination agent will cover all bases. This is not good medicine, and we can do better for our patients.

Dr. Devries: Just to play devil's advocate here, there may still be practitioners out there who are going to say, "OK, it is viral, but the patient still wants some type of treatment." What should we be thinking about in that situation?

Dr. Karpecki: Zirgan (ganciclovir ophthalmic gel 0.15%; Bausch + Lomb) is one option in these cases. It works great.

Dr. Lonsberry: I think the mindset of many practitioners is that the patient wants something, and therefore, I need to give them an eye drop. I think what patients really are asking for, however, is action. They go to their eye care specialist because they want the clinician to do something to address their issue.

What they do not want to hear is, "It's probably viral, so do not do anything." That makes me think that a diagnosis with an objective measurement is as powerful as any antibiotic.

CONTAINING OUTBREAKS

Dr. Karpecki: What about the contagious nature of the infection? Why are the Red Eye protocol and testing for adenovirus important for addressing these issues? Will the isolate be all over the technician and lead to possible contamination? It is important to keep in mind that adenovirus is a potential airborne contaminant that can live on surfaces for 30 to 60 days.

Dr. Epstein: Ask any optometrist who has been infected with EKC. People forget that EKC is the gift that keeps on giving.

Dr. Devries: Or any optometrist who has been involved in class action lawsuits because all their patients got it, and the community became involved because they were convinced it could have been prevented.

Dr. Lonsberry: The concept of the red eye room is not necessarily that you have an examination space where no other kinds of patients are seen; it is more so that wherever the patient is placed is where he or she stays until the test is done.

Dr. Devries: That is where I can see the evolution of the red eye room at our practice. We cannot be moving patients around. I would think that clinics that do not have a dedicated red eye room could modify the way they handle the protocol for their office. The protocol means training personnel and staff to assume a case is contagious until evidence proves otherwise.

Dr. Karpecki: Yes, because rooms that have held EKC-infected patients require special cleaning.

Dr. Melton: My staff is trained to administer the AdenoPlus test if they see a patient with conjunctivitis. Often, the results are ready by the time I get to the examination room.

Dr. Karpecki: That is the way I do it, as well. I require my staff to do it. When I decided to implement the Red Eye Protocol, I provided training on how to perform the AdenoPlus test, and I instructed them to do it on every red eye before any other testing.

When I encountered the first patient with bilateral red eyes that came in without having the test performed, rather than repeat the instructional course, I simply asked my technician to do the test. For the first three cases, none of them did it, but now they all do it for all red eyes ahead of time. They have become very proficient regarding when to administer the test.

MOTIVATING FACTORS FOR IMPLEMENTING THE RED EYE PROTOCOL AND TESTING

Dr. Karpecki: Panelists, what is motivating you to use the Red Eye Protocol with the AdenoPlus test? There are several reasons to be interested in this kind of test: it is a potential practice builder, it helps prevent infection for the clinic and for patients, parental buy in, and it aids in choosing appropriate therapy. This last point highlights how optometry fits into the larger medical community, because if we are disciplined about when we prescribe antibiotics, we are not contributing to the growing problem of antibiotic resistance in the community.

Dr. Brujic: For me personally, this is about best clinical practices, which will ultimately lead to best outcomes, which will ultimately lead to best practice outcomes. It is a very easy equation: Put everything in the best interest of the patient, which is what we are doing with this protocol and this test, and then everything else will follow.

Dr. Devries: I agree from the standpoint that this is something that is going to be standard of care within practices within a very short period of time. I think that

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is why it is important to get involved ahead of time and to have this protocol installed, because it is going to attract more patients and referral sources. It is my sense that eventually, it is going to be standard of care, like strep testing.

Dr. Melton: The primary motivator for me is to identify a potential contagious eye infection that is going to alter your management plan for a patient. Being able to identify whether a case is adenovirus or not is crucial in this regard.

Dr. Kabat: Although I think the motivation for many eye care physicians to adopt the AdenoPlus test and Red Eye Protocol will be practice building and competitive advantage, I hope that most will also realize that point-of-care testing for acute conjunctivitis is going to become the standard of care because of the time and cost savings to patients and clinics alike. It is the level of care we should be providing our patients.

Dr. Lonsberry: To me, the most important aspect of all of this is having the Red Eye Protocol so that everyone in the office—doctors, staff, technicians, personnel—are on the same page about how to handle infectious disease. When a patient presents to the clinic with a red eye, he or she wants effective care. Having a protocol in place establishes the optometrist and his or her staff as the local experts in the management of red eye.

Dr. Nichols: What influenced me was hearing practitioners say, “I was wrong.” That is a powerful motivator, because if the colleagues who I trust and admire for their diagnostic acumen can be wrong, what about me? My fear of misdiagnosing patients drove me to try the AdenoPlus test and adopt the Red Eye Protocol.

Dr. Kading: The AdenoPlus test’s main strength is

that it is a fast, reliable, and accurate way to diagnose patients. It gives our patients confidence in our diagnosis. In the past, each of us has sent kids back to school or adults back to work based on a fairly certain diagnosis. This protocol and test enable us to do better now.

Dr. Karpecki: That feeling of diagnostic confidence is crucial, and this test and protocol are tools to give us that.

Dr. Epstein: I recently started building a new practice from the ground up based on my 30 years of experience. For me, this is a practice differentiator. We are going to differentiate our practice with tools like AdenoPlus and the Red Eye Protocol, because I believe that I have a responsibility to manage patients to the highest level possible. I think these tools will also open up doors to get referrals from pediatric and primary care practices.

From an overarching perspective, our insecurities make us very patient centric. It motivates us to learn to go the extra mile, and so anything that will give an optometrist a level of confidence to move forward is a good thing. Technology like this will make our profession more confident. ■

1. O'Brien TP, Jeng BH, McDonald M, Raizman MB. Acute conjunctivitis: truth and misconceptions. *Curr Med Res Opin.* 2009;25(8):1953-1961.

2. Leibowitz HM, Pratt MV, Flagstad JJ, et al. Human conjunctivitis. *Arch Ophthalmol.* 1976;94:1747-1749.

3. Stenson S, Newman R, Fedukowicz H. Laboratory studies in acute conjunctivitis. *Arch Ophthalmol.* 1982;100:1275-1277.

4. Fitch CP, Rapoza PA, Owens S, et al. Epidemiology and diagnosis of acute conjunctivitis at an inner-city hospital. *Ophthalmology.* 1989;96:1215-1220.

5. Rietveld RP, ter Reit G, Bindels PJ, et al. Predicting bacterial cause in infectious conjunctivitis. *BMJ.* 2003;324(7459):206-210.

6. Rietveld RP, van Weert HC, ter Reit G, Bindels PJ. Diagnostic impact of signs and symptoms in acute infective conjunctivitis. *BMJ.* 2003(7418):789.

7. Solomon AS. Symptoms of allergic conjunctivitis. *Arch Ophthalmol.* 1985;103(7):891.

8. Kosirukvongs P, Visitsunthorn N, Vichyanond P, et al. Allergic conjunctivitis. *Asian Pac H Allergy.* 2001;19:237-244.

9. Gordon Y. Adenovirus and other nonherpetic viral diseases. In: Smolin G, Throft R, eds. *The Cornea*, 3rd ed. Boston: Little, Brown, 1994:215-218.

10. Marangon FB, Miller D, Alfonso E. Laboratory results in ocular viral diseases: implications in clinical-laboratory correlation. *Arq Bras Oftalmol* 2007; 70:189-194.

11. Data on file, Nicox, Inc.