A key part of the many debates over health care is the idea of providing the best possible care with increasingly limited resources. This attention to spending has amplified the interest in more cost-conscious medicine. A 2012 report in the Journal of the American Medical Association identified six areas of medical waste and, among these, overtreatment (including superfluous testing, treatments or hospitalizations) was the biggest of the offenders, with estimates of $150 to $225 billion wasted by such activities in the United States annually.\(^1\) Lost in these arguments, at times, is that no matter the dollar figures involved, such activities are often bad medicine as well as bad economics. So perhaps a silver lining that may emerge from the chaos that is health-care reform is the reaffirmation that in medicine, as in many other vocations, less is very often more.

An example of this is the Choose Wisely campaign,\(^2\) an effort spearheaded by the American Board of Internal Medicine that has recruited more than 50 specialty societies, including the American Academy of Ophthalmology, to identify tests and procedures that are overused, provide little clinical benefit and, in some cases, may even be obstacles to achieving the best possible patient outcomes. These groups identified five or more suggested practices based upon the latest in evidence-based assessments. One of the AAO recommendations states, “Don’t perform preoperative medical tests for eye surgery unless there are specific medical indications.” So unless the patient has a history of heart disease, for example, a preoperative EKG is unnecessary. Some of the Choose Wisely recommendations run counter to established practices, but in a sense, that’s the point: They are a way of rethinking standard operating procedures in light of 21st-century economics and, most importantly, 21st-century medical evidence.

In this month’s column we examine selected front-of-the-eye diagnostics and standard operating procedures and ask how these procedures hold up to a “choose wisely” inspired evaluation. Our strong bias in this discussion is that patient history and examination remain the most valuable sources of information for diagnostic inquiry.

Which Conjunctivitis?

Acute conjunctivitis presents with a spectrum of features that will often provide all the diagnostic data needed to determine the underlying etiology.\(^3\) What we like to refer to as “Abelson’s diagnostic triad” states that if it’s itchy, it’s allergy; if it’s sticky, it’s bacterial; and if it burns it’s dry eye. Clear discharge, visual impairment, photophobia and ocular pain are other features that can be useful in whittling down the diagnosis.\(^4\) Viral conjunctivitis can have a variable presentation, but a key to remember is that it’s typically follicular, so swollen lymph nodes (especially periauricular nodes) can be diagnostic. These initial assessments can be followed up by additional testing, exploratory therapeutics or both.

While a test dose of a topical antihistamine is probably the most efficient way to confirm a diagnosis of allergic conjunctivitis, other forms of conjunctivitis may require further investigation. Another of the AAO recommendations in the Choose Wisely campaign is “Don’t order antibiotics for adenoviral conjunctivitis (pink eye).” Despite this, recent
estimates suggest that physicians (including ophthalmologists) are not particularly adept at discriminating between bacterial or viral etiologies. With the exception of severe cases, culturing of bacteria or viral infections is neither time- nor cost-effective. A simple, rapid test for adenovirus (Adenoplus, RPS Inc.) can help define a diagnosis when there is a question of viral vs. bacterial etiology. It's worth remembering that about 80 percent of acute conjunctivitis cases are viral, and of these, between 65 to 90 percent are due to one of the adenovirus serotypes (as discussed in Therapeutic Topics, March 2010). The Adenoplus test can minimize misuse of antibiotics, and also can confirm the need for patient isolation to prevent the spread of virus.

Dry-Eye Diagnostics

The diagnosis of dry eye is complex; the condition can result from any number of causes (or combinations of causes), each of which contributes to the patient’s presentation. Thus, patients with an aqueous deficiency of the tear film will present different symptomology from those with meibomian gland disease, but all are likely to share some degree of discomfort, surface inflammation and visual impairment. Diagnosis has traditionally been made using the combination of patient symptomology, tear assessments using Schirmer’s strips and ocular surface staining. Lack of a reproducible, consistent association between signs and symptoms of dry eye represents the single biggest impediment to both accurate diagnosis and development of effective treatments.

The diagnostic tests for dry eye described in the International Dry Eye Workshop include measures of tear volume (Schirmer’s test, phenol red thread test and meniscus height), physical properties (breakup times, osmolarity), composition (lactoferrin) and tear dynamics (turnover rate). Review of the evidence behind each of these methods indicates that none alone provides the sensitivity and specificity needed for a reliable diagnostic. Without a diagnostic gold standard, the recommendations of the DEWS report leave both practitioners and clinical researchers to rely on the “tetrad” of symptom questionnaires, corneal staining, tear-film breakup and Schirmer’s test as the most reliable means of dry-eye assessment. Research at Ors has led to the development of a number of refinements to tear-film assessments, but these are generally not suited for routine clinical practice. It seems that none of these traditional metrics is a particularly wise choice, since none provides a robust metric from which to derive a therapeutic strategy. Despite this, new technologies are available or in development that attempt to address this unmet need.

Use of imaging techniques is one such area of diagnostic progress. Established technologies such as optical coherence tomography or confocal microscopy are being adapted to examine tear-film properties, corneal nerve structures, inflammatory cell infiltration and structure of meibomian glands. These methodologies allow for a more precise assessment of the tear film, and provide the means to monitor the cellular morphology associated with dry eye. It’s likely that with additional studies revealing changes in the epithelium, meibomian glands and corneal nerves associated with dry eye (both aqueous-deficient and MG disease), it will be possible to use these imaging modalities for objective diagnosis and treatment monitoring.

Analyzing Tear Components

Efforts at characterizing tear protein components, and the potential use of protein profiling as a diagnostic tool, go back several decades. These efforts mirror the difficulty of developing efficacious treatments, and there are still few validated tear biomarkers for dry eye; major candidates include several pro-inflammatory cytokines, metalloproteinases or lactoferrin. Several new devices designed for use in clinical practice are available that offer the ability to analyze tear constituents as a diagnostic for dry eye. One of these, InflammaDry (RPS), measures the concentration of matrix metalloproteinase 9 in a simple, one-step device similar to the Adenoplus. This protease is involved in the breakdown of epithelial integrity associated with chronic inflammation.
(ATD), another one-step system to measure either tear lactoferrin or IgE levels is also now on the market. It’s thought that a comparison of markers of inflammation (lactoferrin or MMP 9) with a primary marker of ocular allergy (IgE) will help distinguish between dry eye and chronic allergy, though proof of the utility of these devices will only come from clinical studies that track the biomarkers as a function of therapeutic regimes or correlative biomarkers to other signs and symptoms. There are promising studies that suggest that elevated MMP 9 levels in tears are an early predictor of dry eye, and that the levels of the protease in tears show a significant correlative to other dry-eye signs and symptoms. However, there are several issues with the use of MMP 9 tests for dry eye that clinicians need to be aware of, including the reported effects of contact lens use and prostaglandin analogues on tear levels of the protease. Despite these potentially confounding issues, the MMP 9 test does appear to have value as an objective measure of ocular surface inflammation.

Another tear composition diagnostic that’s now widely available is the TearLab Osmolarity Test (TearLab), a device that measures the concentration of tear solutes and is described as an objective, reliable measure of the severity of dry-eye disease. Despite this claim, there are limitations to the use of osmolarity as a diagnostic for dry eye. For instance, compensatory mechanisms, such as more rapid blinking, can significantly alter tear osmolarity, as can other factors such as patient hydration, diurnal variation, environmental conditions and other diagnostic procedures. While some have described osmolarity as the “gold standard” of dry-eye diagnostics, it’s clear that currently available measures of osmolarity alone cannot unequivocally confirm or disprove a diagnosis of dry eye. In fact, the FDA indication for TearLab describes it as an “aid in the diagnosis of dry-eye disease in patients suspected of having dry-eye disease, in conjunction with other methods of clinical evaluation.”

The value of osmolarity measurements in monitoring treatment is also unclear. In a recent retrospective study, Francisco Amparo, MD, and his colleagues at the Schepens Eye Research Institute compared osmolarity values to other measures of dry eye, including the ocular surface disease index survey and Oxford-scale rated corneal staining. They report that while there was modest correlation between osmolarity and the more traditional measures of dry eye, there was no correlation between changes in osmolarity and improvements in OSDI or staining scores. While an alternative interpretation of this study was also recently published, it is nonetheless hard to see how a test with a Food and Drug Administration indication to be used in conjunction with other dry-eye metrics can be considered a gold standard for either clinical diagnosis or as an endpoint (or inclusion criteria) for clinical trials.

Some of these newer technologies may provide value in diagnosis and formulation of the best treatment plans. When we consider any new diagnostics, however, remember to consider several key factors: Does the result of the test improve our ability to render an accurate diagnosis? Can the test be used to follow or modify the course of a patient’s condition? If not, then what is its value? We are reminded of the Yogi Berra aphorism that, sometimes, “You can observe a lot just by watching.” While there are a number of powerful, technologically sophisticated new devices either on the market or under development that will all claim to provide the key to diagnostic success, no machine has been invented that can supplant the value of a thorough patient history and exam. So, it’s up to us to choose wisely when mapping the course for diagnosis and management of all ocular surface diseases.

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