DRY-EYE TESTS
Four diagnostic technologies to watch in the next five years

by Howard Larkin in Chicago

Recent technologies make possible precise measurement of many clinical characteristics of dry eye, moving closer to objective diagnosis of this ocular condition. Presenters at the 2012 ASCRS Cornea Society Cornea Day highlighted four that they believe could become primary diagnostic tests within five years.

Ocular surface interferometer
According to the International Workshop on Meibomian Gland Dysfunction (MGD), MGD may be the leading cause of dry eye disease throughout the world (Nichols et al. Invest Ophthalmol Vis Sci 2011; 52(4):1922-1929), said Richard S Davidson MD, of the University of Colorado, US. A study in press of one clinic found that 86 per cent of dry-eye cases involved lipid deficiency compared with 14 per cent aqueous deficiency, he added. Decreased lipid secretions associated with MGD increase tear evaporation by four to 16 times, leading to decreased aqueous layer thickness, unstable tear film and dry eye symptoms, Dr Davidson noted. But in up to half of cases, MGD is not obvious from visual examination, though expressing the glands often can reveal non-obvious MGD, which may appear as thick, non-liquid lipid secretions.
The ocular surface interferometer provides a means to precisely measure tear film thickness and quantify lipid levels in the tear film. This enables not only objective initial diagnosis of MGD, but also tracking progression and treatment response, Dr Davidson said. Using images collected in a non-contact 20-second scan, the device calculates interferometric colour unit statistics on a frame-by-frame basis, processing about one billion data points.

Osmolarity test
Hyperosmolarity, which often results from excessive tear evaporation disrupting normal ion concentrations, is a common finding across all forms of dry eye diseases, said Reza Dana MD, MPH, MSc, of Harvard Medical School, Boston, US. Increased osmolarity also has been shown to cause ocular surface epithelial cell death by initiating apoptosis cascade, cause inflammation and up-regulate inflammatory cytokines.
Osmolarity can easily be measured using the hand-held TearLab device, which collects a minute quantity of tear from the ocular surface and instantly tests it, and is much less cumbersome than traditional corneal staining or Schirmer strip tests, Dr Dana said.
In tests, osmolarity also correlates more closely with dry eye severity than staining or Schirmer tests, with an R² coefficient of 0.5538 for osmolarity compared with 0.4339 for staining and 0.1698 for Schirmer (Sullivan B et al. IOVS 2010). However, a retrospective study of 378 subjects at Harvard showed that osmolarity did not correlate well with corneal staining or symptom change in response to therapy, and osmolarity was highly variable whether symptoms improved or worsened, Dr Dana said.
“Tear film osmolarity is an easy-to-use, standardised test that can be very helpful in the diagnosis of dry eye disease, especially in the mild-to-moderate range. It has, however, some limitations in predicting changes in symptoms and corneal staining in response to therapy,” Dr Dana said.

MMP-9 inflammatory marker
Because it detects an important chemical marker of inflammation in distressed epithelial cells, whether inflammation is visible or not, a test for metalloproteinase 9, or MMP-9, may help objectively identify dry eyes, said Stephen Kaufman MD, PhD, of the University of Minnesota, Minneapolis, US. “It is a tool to help diagnose dry eye disease in patients who do not demonstrate the classic clinical findings of the condition.”
Many studies have described the association of MMP-9 with dry eye, Dr Kaufman noted. A new clinical device from Rapid Pathogen Screening that draws a small quantity of tear fluid allows detection of this compound, which is expressed in the presence of ocular inflammation. A company test showed the system has 92 per cent specificity and 87 per cent sensitivity, much higher than existing diagnostic tests. The test is positive when it detects more than 40 ng/mL MMP-9 in tear fluid. This makes it sensitive enough to detect MMP-9 even in dilute tears. However, in early dry eye the test may not be positive if no inflammation has developed.
Elevated MMP-9 levels indicate a patient may respond to anti-inflammatory treatments, such as corticosteroids, cyclosporine and doxycycline, Dr Kaufman said. The device also could be useful in assessing dry eye treatment.

High-resolution OCT
Because the eye is available for inspection, imaging the ocular surface may be the easiest way to make a diagnosis, said Victor L Perez MD, of the University of Miami School of Medicine. He presented an ultra-high resolution optical coherence device operating at 840 nm central wavelength capable of 3.0 micron resolution at 24 frames per second. This allows quantitative and qualitative assessment of epithelium thickness, and tear film integrity and break-up. Dr Perez and colleagues observed that the corneal epithelium is bumpy, and has coined a term called the epithelial irregularity factor (EIF), which is defined as the standard deviation of epithelial thickness in the central 3.0mm of the cornea. Preliminary data suggests the EIF correlates with subjective dry eye symptoms (r=0.88), and with corneal fluorescein staining (r=0.55).
Once we optimise and validate the measure we hope the EIF may help identify dry eye patients. We also have noted in very preliminary data that EIF values decline in response to treatment, he noted, leading to the possibility that the EIF may be used to monitor patient response to therapy.
“EIF could be a novel qualitative and quantitative criterion for diagnosing and follow-up of dry eye,” Dr Perez said. He predicted that in five years it could be an objective indicator of the clinical symptoms of dry eye patients.

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