

# A New Diagnostic Test for Dry Eye Disease

An immunoassay test helps ophthalmologists manage dry eye disease and optimize surgical outcomes.

**BY ERIC D. DONNENFELD, MD**

Ocular surface disease is the most common problem that ophthalmologists encounter, and it is frequently associated with dry eye disease (DED). Dry eye is complex, involving a combination of aqueous tear deficiency and evaporative stress that leads to inflammation and hyperosmolarity. The discordance between symptoms, clinical signs, and diagnostic test results makes the diagnosis and treatment of DED challenging.<sup>1</sup>

DED is one of the most frequent complications of ocular surgery, particularly LASIK.<sup>2,3</sup> It is also a common problem after cataract surgery, especially when the procedure involves limbal relaxing incisions. It is more frequent in older patients undergoing cataract surgery, and the incisions and medications can worsen preexisting or barely compensated for dry eye symptoms. Most importantly, patients with DED are more prone to suboptimal visual results with their refractive corneal and cataract surgery than individuals without the disease.

Some asymptomatic patients with no history of DED develop very troublesome symptoms, whereas others experience none at all. Worse still, preoperatively distinguishing between these two types of patients can prove difficult with traditional diagnostic tools. The ability to diagnose DED and then counsel and treat the patient, however, has never been more important.

## IMMUNOASSAY TEST

The nonspecific inflammatory marker matrix metalloproteinase 9 (MMP-9) has consistently been shown to be elevated in the tears of patients with DED. MMP-9 plays a critical role in wound healing and inflammation.<sup>4,5</sup> It is primarily responsible for the pathologic alterations to the ocular surface that lead to a dysfunctional tear film.<sup>4,6</sup> MMP-9 activity is significantly elevated, even in mild DED, and may be a more sensitive diagnostic marker than clinical signs. Furthermore, the level of MMP-9 in



**Figure.** InflammDry, an in-office immunoassay test, detects elevated MMP-9 in patients' tears. It is currently under FDA 510(k) review.

tears correlates with the clinical severity of the disease.<sup>7</sup> InflammDry (Rapid Pathogen Screening Inc.) is a new, in-office immunoassay that detects elevated MMP-9 in tears in 10 minutes (Figure). This test is currently under FDA 510(k) review but is available outside the United States. Identifying patients with inflammatory dry eye is the first step to better perioperative management of the ocular surface.

## DRY EYE AFTER LASIK

LASIK surgery is the most commonly performed vision correction surgery in the United States<sup>8</sup> and postoperative DED is a major cause of dissatisfaction.<sup>9-11</sup> Although the problem is usually short-lived, rarely, patients complain of severe symptoms.<sup>12,13</sup> Other complications such as fluctuating vision, decreased BCVA, and severe discomfort may occur.<sup>14</sup>

Corneal wound healing after LASIK may be prolonged because of the insufficient attachment between the corneal flap and the corneal bed,<sup>15</sup> and it is associated with

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elevated levels of MMP-9.<sup>16</sup> Both dislocation of corneal flaps<sup>17,18</sup> and ectasia<sup>19</sup> after LASIK appear to be related to corneal wound healing. Also, post-LASIK epithelial ingrowth is associated with elevated MMP-9.<sup>16</sup> The incidence of epithelial ingrowth is about 1% after LASIK<sup>20</sup> and develops in the interface through one of two known mechanisms: epithelial invasion and epithelial implantation. Compared with patients not suffering from DED, the post-operative health of the ocular surface in individuals with preexisting tear dysfunction is poorer. The latter also have more severe symptoms of tear dysfunction after LASIK, and their corneal sensitivity takes longer to recover.<sup>21-23</sup>

Nevertheless, patients with preexisting mild to moderate DED can safely undergo LASIK after optimization of their ocular surface. In some cases, care of the ocular surface must continue after surgery.<sup>21,24-25</sup> Management of the ocular surface during LASIK (as well as long-term management of the tear film and ocular surface) can minimize damage and the risk of adverse outcomes, leading to a reduction in the severity and duration of dry eye symptoms and signs.<sup>23</sup> Konomi et al suggested that topical anti-inflammatory therapeutics could normalize the ocular surface and improve the quality of the tear film after LASIK.<sup>26</sup>

### TREATMENT OPTIONS AFTER DIAGNOSIS

In DED, the eye can be white and quiet despite an inflamed tear film. Elevated levels of MMP-9, especially in the setting of artificial tears' not being effective, confirms the diagnosis of DED and should trigger the use of anti-inflammatory therapies such as cyclosporine. Because DED is a progressive disorder, the earlier treatment is started, the better the response to therapy will be.<sup>27</sup> Sometimes, a short course of topical steroids used simultaneously with the initiation of cyclosporine will help reduce the sting, allow for rapid symptomatic relief, and facilitate better long-term adoption of cyclosporine.<sup>28</sup> If additional treatment such as punctal occlusion is required, identifying and treating patients with ocular inflammation first prevents the potential accumulation of inflamed tears that may exacerbate the ocular surface disease. A negative InflammDry test suggests a non-inflammatory cause of DED. At this point, the clinician should evaluate all of the clinical information to determine the best course of action.

### CONCLUSION

The perioperative optimization of the ocular surface may improve the outcome of and reduce complications from LASIK and cataract surgery. When available in the United States, the InflammDry should allow clinicians to make better treatment decisions. ■

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1. Wilson SE, Stulting RD. Agreement of physician treatment practices with the international task force guidelines for diagnosis and treatment of dry eye disease. *Cornea*. 2007;26(3):284-289.
2. De Paiva CS, Chen Z, Koch DD, et al. The incidence and risk factors for developing dry eye after myopic LASIK. *Am J Ophthalmol*. 2006;141:438-445.
3. Shojja MR, Besharati MR. Dry eye after LASIK for myopia: incidence and risk factors. *Eur J Ophthalmol*. 2007;17:1-6.
4. McCollum C, Foulks G, Bodner B, et al. Rapid assay of lactoferrin in keratoconjunctivitis sicca. *Cornea*. 1994;13:505-508.
5. Pflugfelder SC, Jones D, Ji Z, et al. Altered cytokine balance in the tear fluid and conjunctiva of patients with Sjögren's syndrome keratoconjunctivitis sicca. *Curr Eye Res*. 1999;19:201-211.
6. Alfonso A, Sobrin L, Monroy DC, et al. Tear fluid gelatinase B activity correlates with IL-1a concentration and fluorescein tear clearance. *Invest Ophthalmol Vis Sci*. 1999;40:2506-2512.
7. Chotikavanich S, de Paiva CS, Li de Q, et al. Production and activity of matrix metalloproteinase-9 on the ocular surface increase in dysfunctional tear syndrome. *Invest Ophthalmol Vis Sci*. 2009;50:3203-3209.
8. Duffey RJ, Leaming D. US trends in refractive surgery: 2004 ISRS/AAO survey. *J Refract Surg*. 2005;21:742-748.
9. Hovanesian JA, Shah SS, Maloney RK. Symptoms of dry eye and recurrent erosion syndrome after refractive surgery. *J Cataract Refract Surg*. 2001;27:577-584.
10. Bailey MD, Mitchell GL, Dhaliwal DK, et al. Reasons patients recommend laser in situ keratomileusis. *J Cataract Refract Surg*. 2004;30:1861-1866.
11. Jabbur NS, Sakatani K, O'Brien TP. Survey of complications and recommendations for management in dissatisfied patients seeking a consultation after refractive surgery. *J Cataract Refract Surg*. 2004;30:1867-1874.
12. Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. *Cornea*. 2006;25:900-907.
13. Berry S, Mangione CM, Lindblad AS, et al. Development of the National Eye Institute refractive error correction quality of life questionnaire: focus groups. *Ophthalmology*. 2003;110:2285-2291.
14. Ambrosio R. LASIK-associated dry eye and neurotrophic epitheliopathy: pathophysiology and strategies for prevention and treatment. *J Refract Surg*. 2008;24:396-407.
15. Mutoh T, Nishio M, Matsumoto Y, et al. Correlation between the matrix metalloproteinase-9 activity and chondroitin sulfate concentrations in tear fluid after laser in situ keratomileusis. *Clin Ophthalmol*. 2010;4:823-828.
16. Fournié PR, Gordon GM, Dawson DG, et al. Correlation between epithelial ingrowth and basement membrane remodeling in human corneas after laser-assisted in situ keratomileusis. *Arch Ophthalmol*. 2010;128:426-436.
17. Nowroozzadeh MH. Early flap dislocation with perioperative bromonidine use in laser in situ keratomileusis. *J Cataract Refract Surg*. 2010;36:368.
18. Oh-i K, Mori H, Kubo M, et al. LASIK flap dislocation by blunt trauma seven weeks after surgery. *J Refract Surg*. 2005;21:93-94.
19. Esquenazi S, Esquenazi I, Grunstein L, et al. Immunohistological evaluation of the healing response at the flap interface in patients with LASIK ectasia requiring penetrating keratoplasty. *J Refract Surg*. 2009;25:739-746.
20. Schallhorn SC, Amesbury EC, Tanzer DJ. Avoidance, recognition, and management of LASIK complications. *Am J Ophthalmol*. 2006;141:733-739.
21. Toda I, Asano-Kato N, Hori-Komai Y, et al. Laser-assisted in situ keratomileusis for patients with dry eye. *Arch Ophthalmol*. 2002;120:1024-1028.
22. Yu EY, Leung A, Rao S, Lam DS. Effects of laser in situ keratomileusis on tear stability. *Ophthalmology*. 2000;107:2131-2135.
23. Albiatz JM, Lenton LM, McLennan SG. Chronic dry eye and regression after laser in situ keratomileusis for myopia. *J Cataract Refract Surg*. 2004;30:675-684.
24. Alio JL, Artola A, Belda JJ, et al. LASIK in patients with rheumatic diseases: a pilot study. *Ophthalmology*. 2005;112:1948-1954.
25. Toda I, Asano-Kato N, Hori-Komai Y, et al. Ocular surface treatment before laser in situ keratomileusis in patients with severe dry eye. *J Refract Surg*. 2004;20:270-275.
26. Konomi K, Chen LL, Tarko RS, et al. Preoperative characteristics and a potential mechanism of chronic dry eye after LASIK. *Invest Ophthalmol Vis Sci*. 2008;49:168-174.
27. Wilson SE, Perry HD. Long-term resolution of chronic dry eye symptoms and signs after topical cyclosporine treatment. *Ophthalmology*. 2007;114(1):76-79.
28. Donnenfeld E, Sheppard J, Holland E, et al. Prospective, multi-center, randomized controlled study on the effect of loteprednol etabonate on initiating therapy with cyclosporin A. Paper presented at: The American Academy of Ophthalmology Annual Meeting; November 10, 2007; New Orleans, Louisiana.