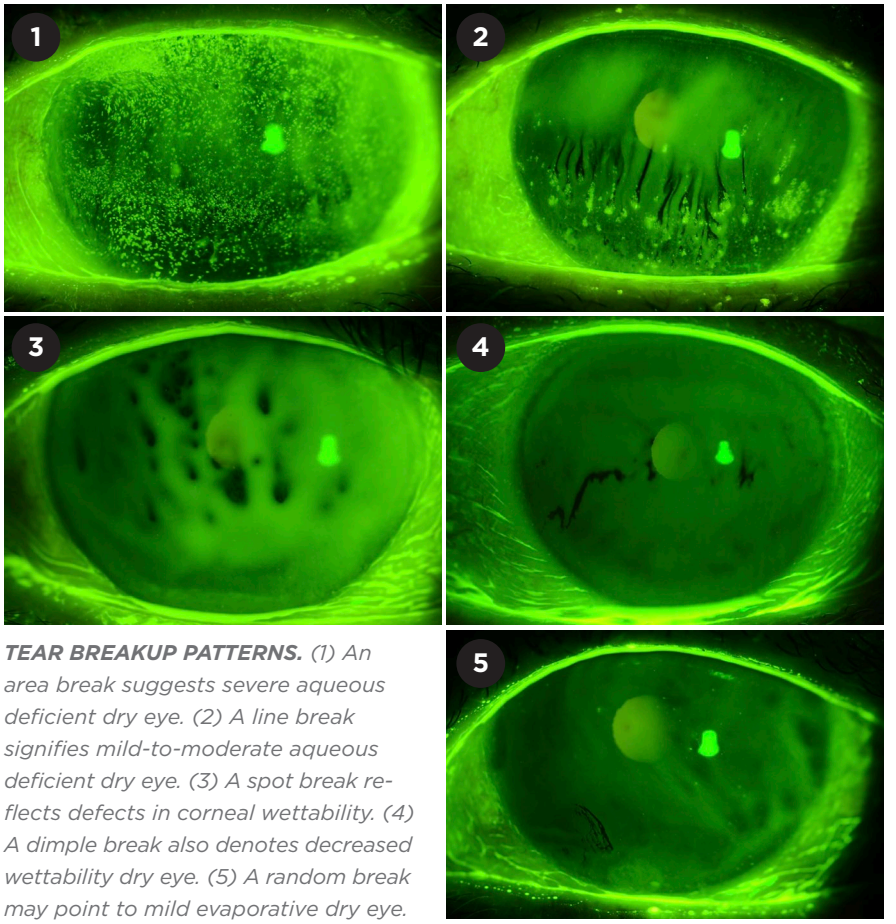
Consensus Report Simplifies Dry Eye Diagnosis

The complexity of dry eye disease (DED) and the growing influx of patients who have it make diagnosing this condition challenging and time-consuming.

To simplify diagnosis, a group of experts from around the world released a clinically oriented consensus definition of DED.[1] They also offered practical ways to consistently diagnose DED and identify the pathophysiology behind individual cases. Moreover, no new equipment is required. As Deepinder K. Dhaliwal, MD, LAc, at the University of Pittsburgh School of Medicine, put it, "All that's needed to diagnose dry eyes are a history, a slit lamp, and a fluorescein strip."



TEAR BREAKUP PATTERNS. *(1) An area break suggests severe aqueous deficient dry eye. (2) A line break signifies mild-to-moderate aqueous deficient dry eye. (3) A spot break reflects defects in corneal wettability. (4) A dimple break also denotes decreased wettability dry eye. (5) A random break may point to mild evaporative dry eye.*

The New Diagnostic Criteria

Why new criteria were needed. In 2016, an international group of experts began discussing the need for a global definition of DED. Stephen Pflugfelder, MD, at Baylor College of Medicine in Houston, joined in the effort. He said that some of the prevailing diagnostic criteria, such as those from the Tear Film and Ocular Surface Society Dry Eye Workshop II (DEWS II),[2] were clinically impractical.

In addition, ophthalmologists in different parts of the world defined DED differently, complicating international clinical trials. For example, DEWS II proposed two types of DED, aqueous deficient and evaporative, which were thought to occur on a spectrum.[2] The Asia Dry Eye Society proposed a third type: decreased wettability dry eye.[3] Patients with this type produce enough tears, but their tears break up quickly due to insufficient or abnormal membrane-associated mucin.

The new definition. After four meetings, the experts issued their definition in a report published in 2020: "Dry eye is a multifactorial disease characterized by a persistently unstable and/or deficient tear film causing discomfort and/or visual impairment, accompanied by variable degrees of ocular surface epitheliopathy, inflammation, and neu-

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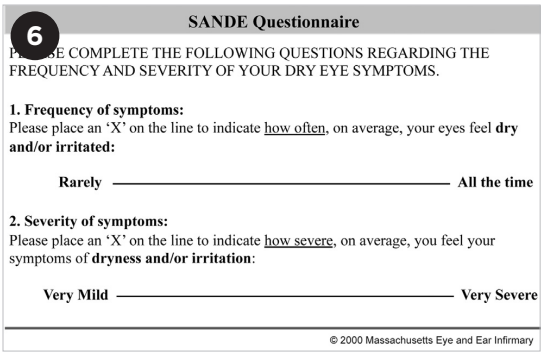

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SANDE Questionnaire

PLEASE COMPLETE THE FOLLOWING QUESTIONS REGARDING THE FREQUENCY AND SEVERITY OF YOUR DRY EYE SYMPTOMS.

1. Frequency of symptoms:
Please place an 'X' on the line to indicate how often, on average, your eyes feel **dry and/or irritated:**

Rarely ——— All the time

2. Severity of symptoms:
Please place an 'X' on the line to indicate how severe, on average, you feel your symptoms of **dryness and/or irritation**:

Very Mild ——— Very Severe

SANDE. *Questionnaires, such as the Symptom Assessment in Dry Eye, can provide a sense of symptom severity.*

rosensory abnormalities."

Notably, this definition revolves around tear film instability or deficiency, which clinicians can easily measure. In fact, the panelists deemed unstable tear film, when accompanied by ocular discomfort or impaired vision, sufficient to diagnose DED. They also recommended checking all dry eye patients for epitheliopathy, inflammation, and neurosensory issues.

Key Symptoms and Signs

Ocular discomfort. "In most cases, ocular discomfort is displayed before DED is diagnosed, and it is critical for monitoring the progression of the condition and response to treatments," the panel wrote.[1] Discomfort greatly affects the daily lives of dry eye patients, especially those who view electronic screens a lot, said panel member Norihiko Yokoi, MD, PhD, at Kyoto Prefectural University of Medicine in Japan. He explained that tear film breakup, friction during blinking, and lid margin problems such as meibomian gland dysfunction can all cause discomfort. Neurologic problems may also contribute.

Pearls. Given the prevalence of DED, Dr. Pflugfelder recommends asking all patients whether they experience symptoms of dry eye. And Dr. Dhaliwal asks patients: "What are the top three things that bother you about your eyes?"

According to the consensus group, taking detailed notes of patients' symptoms and their triggers may reveal the cause.[1] For example, irritation that grows as the day goes on suggests DED, whereas pain that increases in the morning or the middle of the night may indicate recurrent corneal erosions or epithelial basement membrane dystrophy, said Ahmed Al-Ghoul, MD, MBA, at the University of Calgary in Canada.

Questionnaires. Giving patients a questionnaire can help complete the picture. Dr. Pflugfelder said that he often learns more about symptom severity from questionnaires than from what patients say. Dr. Al-Ghoul uses questionnaires to quantify patients' condition at baseline and throughout treatment. Those data guide treatment decisions.

The panel recommended several questionnaires, including one called Symptom Assessment in Dry Eye (Fig. 6).[1] Dr. Pflugfelder uses this visual analog scale in his practice. Its two items instruct the patient to mark a spot on a line corresponding to, first, the frequency of dryness and irritation, and, second, the severity of symptoms.

Visual impairment. Unstable tear film can cause fluctuating visual impairment, which standard vision tests are not designed to detect. According to Dr. Pflugfelder, they test how well people see in high-contrast conditions, but reduced-contrast vision charts are better at detecting blurry vision in DED.

To assess the visual impact of dry eye, Dr. Al-Ghoul deems the history crucial. Questionnaires, like the Ocular Surface Disease Index and the Standard Patient Evaluation of Eye Dryness, shed light on patients' functional visual acuity, he said.

Unstable tear film. Evaluation of tear film stability often starts with determining the fluorescein tear breakup time. Stained tears that break up within 1 or 2 seconds of the last blink suggest the patient has more severe dry eye and/or corneal disease than the typical dry eye patient, said Dr. Pflugfelder.

Tear film breakup patterns. "Once it's established that the patient has unstable tear film, there should be some attempt to identify the underlying problem," Dr. Pflugfelder said. The problem could arise from either the lipid layer or the aqueous layer of the tear film or from the wettability of the corneal surface. Making this determination can be facilitated by tear film–oriented diagnosis.[3]

With this approach, Dr. Yokoi and colleagues used fluorescein staining to study how tear film breaks up. They found five essential breakup patterns that correspond to specific types of DED.[4]

Area breaks and line breaks (Figs. 1, 2) reflect lacrimal gland dysfunction, which results in aqueous tear deficiency and, generally, epithelial damage. Area breaks signify more severe disease than line breaks.

Spot breaks and dimple breaks (Figs. 3, 4) reflect decreased corneal wettability, perhaps due to a disrupted glycocalyx,[3] whose glycoproteins help keep the ocular surface hydrophilic.[5] Both of these patterns are characterized by short breakup times despite normal tear volume and no significant epithelial damage.[4] Spot breaks suggest more severe DED, with nearly instant tear film breakup and a greater impact on patients' lives.[6]

Random breaks (Fig. 5) suggest a compromised secretory mucin and/or lipid layer. The latter points to mild evaporative dry eye, chiefly meibomian gland dysfunction. Like spot and dimple breaks, random breaks in DED are typically accompanied by short breakup times and no epithelial damage.

Pearl. For proper diagnosis, Dr. Yokoi noted that special instructions must be followed. After wetting the fluorescein strip with two drops of saline or artificial tears, the tester should vigorously shake the strip to remove excess liquid before briefly touching the top of the strip to the lower lid margin. Then, the patient should blink several times before softly closing and briskly reopening the eyes.

Other Factors to Assess

Inflammation. "Inflammation is very important, especially in aqueous deficient dry eye," said Dr. Yokoi. He explained that in this type of DED, often seen in Sjögren syndrome, inflammation in the body can afflict the eyes as well. Speaking more generally, the consensus panel described how in-

flammation can perpetuate the vicious cycle of chronic DED.[1]

Dr. Pflugfelder noted that ocular inflammation often presents no overt signs. To check for inflammation, he uses the Quidel InflammaDry test, an immunoassay that flags high levels of matrix metalloproteinase 9 (MMP-9), which he considers one of the best biomarkers for inflammation in DED.

While additional testing for dry eye patients, such as MMP-9 and meibomian gland imaging, can be helpful, said Dr. Dhaliwal, "its important that all eye care providers feel empowered to treat dry eye even if they don't have these tools."

Ocular epitheliopathy. The panel noted that epitheliopathy, common in DED, can disrupt the tear film, impair vision, and increase eye pain.[1] Dr. Pflugfelder said all dry eye patients should be checked for epitheliopathy. To do so, he uses fluorescein dye for the cornea and lissamine green for the conjunctiva. The effects of dryness on the conjunctiva, which supports the cornea, are often overlooked, he said. Yet, he explained, an unhealthy conjunctiva or a decrease of the conjunctiva's mucus-making goblet cells can destabilize the tear film.

Neurosensory abnormalities. Dr. Pflugfelder suspects neurosensory abnormalities in patients who have high scores (60-100) on the visual analog questions despite normal tear breakup time or rapid tear breakup time with a normal appearing corneal epithelium and no corneal or conjunctival dye staining. Usually, he said, the exam reveals unstable tear film without tissue damage, which might normally explain symptoms such as pain or wind sensitivity. "It's like their threshold for sensing pain and discomfort is reduced."

Surgery. Sometimes heightened sensitivity occurs after LASIK or other surgery, said Dr. Al-Ghoul. He considers neurosensory problems in postsurgical patients who report significant pain.

Cornea or CNS? Abnormal pain in DED may result from sensitization of the corneal surface or from the central nervous system, noted Dr. Yokoi. To discern the cause, Dr. Dhaliwal instills a drop of proparacaine. If that relieves the burning or other symptoms, she can treat the ocular surface with a high likelihood of improving symptoms. She refers patients who are not helped by the anesthetic to either a pain management specialist or a primary care provider, who can prescribe medication for central neuropathic pain.

Regardless of the root cause, all patients with possible neurosensory abnormalities need prompt referral to a cornea specialist, said Dr. Al-Ghoul. Left untreated for too long, such abnormalities continue to progress, making it considerably harder to manage these patients. Earlier treatment equals more successful treatment, he said.

Treat the Right Target

The panel recommends tear film–oriented therapy,[3] which aims to stabilize the tear film by restoring components found to be lacking. For example, Dr. Yokoi treats severe aqueous deficiency with punctal plugs. For decreased wettability, Dr. Pflugfelder might prescribe cyclosporine, which boosts the number of conjunctival goblet cells, or varenicline to spur the release of goblet cell mucins.

Controlling inflammation, whether over the long term or during disease flare-ups, is a must to prevent ocular damage and to rein in symptoms, wrote the panel.[1] Dr. Dhaliwal prescribes anti-inflammatories for most of her DED patients, who tend to present with significant disease. Dr. Pflugfelder, on the other hand, saves anti-inflammatories for patients with significant symptoms, moderate-to-severe ocular surface dye staining, or high MMP-9 levels.

Tear film–oriented therapy allows for a tailored approach to treatment, which is of value in a booming market of dry eye therapeutics, said Dr. Dhaliwal.

Simple Methods for a Complex Problem

Dr. Dhaliwal contends that getting to the bottom of dry eye need not be overwhelming. The consensus diagnostic criteria, if applied consistently, can point the way to minimizing ocular damage, she said.

Yet the disease can remain complex, said Dr. Al-Ghoul, and the time may come to dive in and approach the diagnosis of some patients in a more detailed manner. "If we make it too simple, we can end up missing things, so the question becomes, 'When do we make it simple? And when do we go detailed?'"

1 Tsubota K et al. *Int J Mol Sci.* 2020;21(23):9271.
2 Craig JP et al. *Ocul Surf.* 2017;15(4):802-812.
3 Tsubota K et al. *Eye Contact Lens.* 2020;46(1): S2-S13.
4 Yokoi N et al. *Am J Ophthalmol.* 2017;180:72-85.
5 Uchino Y. *Invest Opthalmol Vis Sci.* 2018;59: DES157-DES162.
6 Shigeyasu C et al. *Diagnostics* (Basel). 2020; 10(9):711.

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